ASSESSMENT OF MATERNAL OUTCOMES AND FETAL OUTCOMES SECONDARY TO SYMPTOMATIC URINARY TRACT INFECTION IN PREGNANCY.

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF M.D. GENERAL MEDICINE BRANCH I EXAMINATION OF THE TAMIL NADU DR. M.G.R. UNIVERSITY, CHENNAI TO BE HELD IN MAY, 2019

CERTIFICATION

This is to certify that the dissertation **"Assessment of maternal outcomes and fetal outcomes secondary to symptomatic urinary tract infection in pregnancy."** is a bonafide work of Dr. Anjely Pulparampil Sebastian carried out under our guidance towards the M.D. Branch I (General Medicine) Examination of the Tamil Nadu Dr. M.G.R. University, Chennai to be held in May, 2019.

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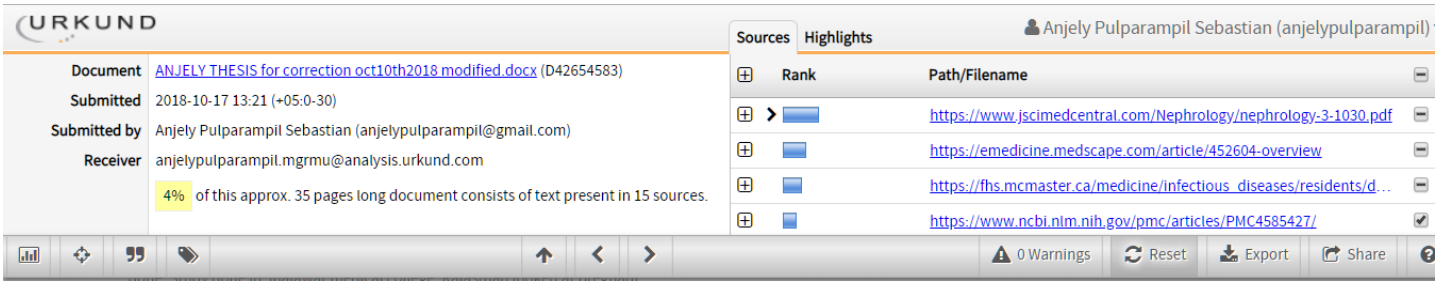

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ABBREVIATIONS

ACOG	American College Of Obstetricians And Gynecologists
CFU	Colony Forming Units
CMC	Christian Medical College
CONS	Coagulase Negative Staphylococci
DM	Diabetes Mellitus
E.coli	Escherichia Coli
ESBL	Extended Spectrum Beta Lactamase

GDM	Gestational Diabetes Mellitus
GPC	Gram Positive Cocci
ICMR	Indian Council Of Medical Research
ICU	Intensive Care Unit
IDSA	Infectious Diseases Society Of America
IL	Interleukin
IQR	Interquartile Range
IUGR	Intrauterine Growth Restriction
LSCS	Lower Segment Caesarean Section
NFGNB	Non Fermenting Gram Negative Bacteria
OGTT	Oral Glucose Tolerance Test
PPROM	Preterm Premature Of Membranes
PROM	Preterm Rupture Of Membranes
SD	Standard Deviation
SES	Socio-Economic Status
UTI	Urinary Tract Infection
VDRL	Venereal Disease Research Laboratory

ABSTRACT

OBJECTIVE:

Primary Objective:

To determine the maternal and fetal outcomes that result from symptomatic urinary tract infection in pregnancy.

METHODS:

This is a cross sectional study which was done in the department of General Medicine and Obstetrics and Gynecology at Christian Medical College Vellore. Pregnant women who were booked in CMC for their antenatal care were included in the study. Pregnant women with symptomatic urinary tract infection with significant growth in urinary culture were taken as cases and others were taken as controls. Maternal and fetal outcomes were assessed at delivery. Comparison of quantitative variables were done using independent t-test or Wilcoxon rank sum test. Comparison of categorical variables were done using Fisher's Exact test. All significant variables were analysed using Logistic regression.

RESULTS AND CONCLUSIONS:

On univariate analysis, preterm premature rupture of membranes was more among the case than controls with OR of 2.697 which was statistically significant (95% CI- 1.423- 5.11, p=0.001) Preterm delivery and post-partum sepsis were also statistically significant with OR of 3.162 and 3.972 respectively. Intrauterine growth restriction, Neonatal ICU admission and low birth weight were more among the infants born to cases than controls which was statistically significant with OR of 1.697, 4.406, and 2.290 respectively.

Primigravida, multifetal pregnancy, low maternal education, past history of catheterization, urinary tract infection, and anemia were statistically significant risk factors for the development of urinary tract infection.

INTRODUCTION

Urinary tract infection (UTI) is a widely prevalent problem in developing countries like India. The prevalence of urinary tract infection is higher in the pregnant women due to the physiological changes that occur in the urinary tract during pregnancy. This leads to adverse maternal and fetal outcomes, which could have been avoided by preventing the urinary tract infection. Despite increase in hospital based ante-natal checkups and more deliveries in hospital than at home which has significantly reduced maternal and fetal morbidity and mortality, maternal and fetal deaths due to complications from urinary tract infection still occur which should ideally be prevented.

The prevalence of bacteriuria is the same in pregnant and non-pregnant women. Pregnant women are at the risk of recurrent bacteriuria. Without treatment, 30 to 40% of these pregnant women will develop symptomatic UTI. By treating asymptomatic bacteriuria in pregnant women, the risk of developing symptomatic UTI can be reduced by 70 to 80% (1). Asymptomatic bacteriuria and symptomatic urinary tract infection are associated with adverse maternal and fetal outcomes such as preterm birth, low birth weight infant, perinatal mortality, sepsis(1,2).

The data from western population shows that the incidence of urinary tract infections is higher in pregnant women and it correlates with adverse maternal and fetal outcomes and it can be prevented by screening for asymptomatic bacteriuria. The Infectious Diseases Society of America (IDSA) and The American College of Obstetricians and Gynecologists (ACOG) guidelines advocate universal screening and treatment of asymptomatic bacteriuria among pregnant women. However, in resource poor and

population dense region as in India, the data on maternal and fetal outcomes with symptomatic UTI is limited. Universal screening for asymptomatic bacteriuria is still not practiced. With increasing incidence of extended spectrum beta lactamase (ESBL) infections in the community, cost of treating a urinary tract infection is significantly higher than screening and treating for asymptomatic bacteriuria.

The aim of this study is to assess adverse maternal and fetal outcomes that occur secondary to symptomatic UTI during pregnancy. The study also aims at looking at the risk factors for UTI, organisms causing UTI and antimicrobial susceptibility pattern of the organisms.

AIMS

The aim of the study is to assess maternal outcomes and fetal outcomes that occur secondary to symptomatic urinary tract infection in pregnancy.

PRIMARY OBJECTIVES

To determine the maternal and fetal outcomes that result from symptomatic urinary tract infection in pregnancy.

SECONDARY OBJECTIVES

1. To determine the risk factors associated with urinary tract infection in pregnancy.
2. To identify the organisms causing UTI.
3. To identify the antimicrobial susceptibility pattern of the organisms.

REVIEW OF LITREATURE

DEFINITION

Urinary tract infection (UTI) is defined as symptoms of UTI in the form of increased frequency of micturition, urgency, lower abdominal pain, and dysuria, with or without fever. It is called complicated urinary tract infection if it occurs in individuals with structural or functional abnormalities of the genitourinary tract like in pregnant women(3).

EPIDEMIOLOGY OF UTI IN PREGNANCY

INCIDENCE

The prevalence of asymptomatic bacteriuria among pregnant women is 1.9 to 9.5% (4) which is similar to that in non-pregnant women. However, pregnant women are at risk of recurrent bacteriuria. The incidence of UTI in pregnancy is higher than in general population in view of anatomical changes that occur during pregnancy. This can be lower urinary tract infection in the form of cystitis or upper urinary tract infection in the form of pyelonephritis. A study done in Wilford Hall USAF medical center which was published in 1981, looked at 9734 deliveries over a 6 year period and showed that the incidence of acute cystitis was 1.3% and 17% of these patients had recurrent urinary tract infection(5). Majority of these patients with acute cystitis had been screened for bacteriuria and had negative urine culture prior to onset of symptom. The most common organism was Escherichia coli and all the patients were treated as outpatients. The incidence of pyelonephritis was 0.5 to 2% as shown in the 18 year retrospective review of medical

records on 546,092 singleton pregnancies delivered in all Kaiser Permanente Southern California hospitals from 1993 through 2010(6). Most cases of pyelonephritis occur during second and third trimesters in this study. This study also showed that African or Hispanic women, younger age of pregnancy, lower education, smoking during pregnancy and delayed initiation of antenatal care was risk factors for urinary tract infection. Pregnant women with pyelonephritis in this study had higher number of spontaneous preterm births, acute kidney injury, septicemia and anemia as compared to the pregnant women without pyelonephritis.

With respect to Indian epidemiology of urinary tract infection in pregnancy, several studies have been done. Study done in Jhalawar medical college, Rajasthan looked at pregnant women with or without symptoms of urinary tract infection. Pregnant women in different stages of pregnancy with or without symptoms of UTI who visited the antenatal clinic from November 2011 to March 2012 were screened for bacteriuria. This study showed significant growth in urine culture in 60 of the 250 samples screened which showed that 24% of the pregnant women in the 5-month study period had significant bacteriuria. The pathogenic organisms isolated were Escherichia coli (E. coli) in 63% and Klebsiella pneumoniae in 8%(7). Among these 60 patients showing significant growth in urine culture, 45 (75%) had asymptomatic bacteriuria and 15 (25%) had symptomatic urinary tract infection(7). In another study done in Aligarh, pregnant women at different stages of pregnancy were screened for bacteriuria with urine culture. It looked at pregnant women with or without symptoms of urinary tract infection. Of all the urine cultures sent, 51.2% (4290/8379) showed significant growth. 74.8% (3210/4290) of these pregnant women were

asymptomatic and 25.2% (1080/4290) were symptomatic for UTI with 51.7% of the gram negative organisms being ESBL producing organisms showing high level antibiotic resistance to cephalosporins. This study showed the higher prevalence of asymptomatic bacteriuria among pregnant women when compared to symptomatic urinary tract infection(8). In these 2 studies, the incidence of asymptomatic bacteriuria was 18% (45/250) in the Jhalawar study and 38% (3210/8379) in the Aligarh study which was significantly higher than that shown in western population studies. Study done by Kant et al in 2017 in Faridabad, Haryana from March 2015 to May 2015, looked at 1253 pregnant women. This study showed the prevalence of asymptomatic bacteriuria of 1.1% and symptomatic bacteriuria was 2.2% with majority of the cases occurring in the third trimester(9).

Table 1: Prevalence of symptomatic bacteriuria across Indian literature

Study name	Prevalence of bacteriuria	Prevalence of Symptomatic bacteriuria
1. Sabharwal et al (2012) (7)	24%	6%
2. Rizvi et al (2011) (8)	51.2%	12.8%
3. Kant S et al (2017)(9)	3.3%	2.2%

RISK FACTORS FOR URINARY TRACT INFECTION

Several studies have been done to assess risk factors for urinary tract infection among pregnant women. Study done in Northwest Ethiopian hospital between January 2011 and April 2011 and published on July 2013, looked at 367 pregnant women of whom 37 had symptomatic urinary tract infection and 330 had asymptomatic urinary tract infection. This study showed that low family income, three or more sexual intercourses per week, past history of UTI and anemia as significant risk factors for UTI. Other risk factors which the study looked at were age of pregnant women, educational status, parity, gestational age, past history of catheterization, and genitourinary abnormality(10). These risk factors were not statistically significant for the development of symptomatic urinary tract infection as per this study.

Diabetes in the form of gestational diabetes mellitus (GDM) is associated with increased risk of urinary tract infection(11). A study done by McMahon MJ et al in 1998, looked at 824 women diagnosed with gestational diabetes mellitus in Canada between 1980 and 1993 had increased incidence of urinary tract infection among pregnant women with GDM as compared to women without GDM (11).

PATHOGENESIS OF URINARY TRACT INFECTION IN PREGNANCY

Female urinary tract system undergoes anatomical and physiological changes during pregnancy(12). The changes that occur are summarized in the table 2 below.

Table 2: Urinary tract changes in pregnancy

SITE	CHANGE
Kidneys	- Increased renal length. - Increased glomerular filtration rate by 30 to 50%.
Collecting system	- Decreased peristalsis.
Ureters	- Decreased peristalsis. - Mechanical obstruction.
Bladder	- Displaced anteriorly and superiorly. - Smooth muscle relaxation. - Increased capacity.

Data from Waltzer WC. The urinary tract in pregnancy. J Urol 1981(13)

During pregnancy, there is hyperprogesteronemia that causes smooth muscle relaxation and decreased peristalsis in the ureters and collecting system. This along with the mechanical obstruction due to the gravid uterus causes mild hydroureteronephrosis which can be seen as early as 7th week of gestation (12).

The prevalence of asymptomatic bacteriuria in pregnancy is almost the same as in non-pregnant women. However, pregnant women are at increased risk of recurrent bacteriuria. Kass et al in 1960, has shown that asymptomatic bacteriuria during pregnancy predisposes to the development of pyelonephritis and asymptomatic bacteriuria if treated appropriately

can prevent development of symptomatic urinary tract infection. Kass et al showed that the presence of bacteriuria in an obstructed system caused an accelerated ascend of infection and pyelonephritis(13,14). In pregnancy, the gravid uterus can exert pressure on the bladder which can simulate an obstructed system. Pregnancy is also associated with immunomodulation as shown by Petersson et al in 1994 who looked at antibody response to E.coli antigen between pregnant and non-pregnant women. He looked at antibody activity and Interleukin 6 (IL-6) in serum and urine.

Antibody	Antibody activity (median and range)		
	At diagnosis	After 2 weeks	P^a
Serum[b]			
Non-pregnant			
IgG	84.5 (29–166)	107 (63–369)	0.001
IgA	127 (36–809)	298.5 (78–6897)	0.001
IgM	57.5 (9–558)	159.5 (19–3786)	0.001
Pregnant			
IgG	64 (22–116)	75 (29–120)	0.005
IgA	67 (5–153)	114 (21–452)	0.019
IgM	37 (19–77)	65 (24–335)	0.003
Urine[c]			
Non-pregnant			
IgG	126 (0–1299)	78.5 (0–1216)	0.001
IgA	54.5 (9–838)	50 (0–1966)	0.001
Pregnant			
IgG	31 (0–210)	56 (0–250)	0.043
IgA	35 (0–149)	54 (0–304)	NS

[a] *P* value for the difference in paired samples in individual patients at the two dates (Wilcoxon signed rank test; significance <0.05). NS is not significant.
[b] Serum antibody activity given in percent of the control.
[c] Urinary antibody activity given as the absorbance at 405 nm after 100 minutes incubation with substrate.

Figure 1.Antibody activity in serum and urine at the time of diagnosis and two weeks later. Adapted from Suppressed antibody and interleukin-6 responses to acute pyelonephritis in pregnancy. Petersson et al. 1994.(15)

This study showed that pregnant women had lower levels of immunoglobulin G, immunoglobulin M and immunoglobulin E in serum and urine as compared to non-pregnant women which was seen at the time of diagnosis of acute pyelonephritis and also after 2 weeks. It also looked at change in antibody activity in serum and urine among non-pregnant and pregnant women with acute pyelonephritis. It showed that the change in antibody activity was higher in the non-pregnant women as compared to the pregnant women and it was statistically significant.

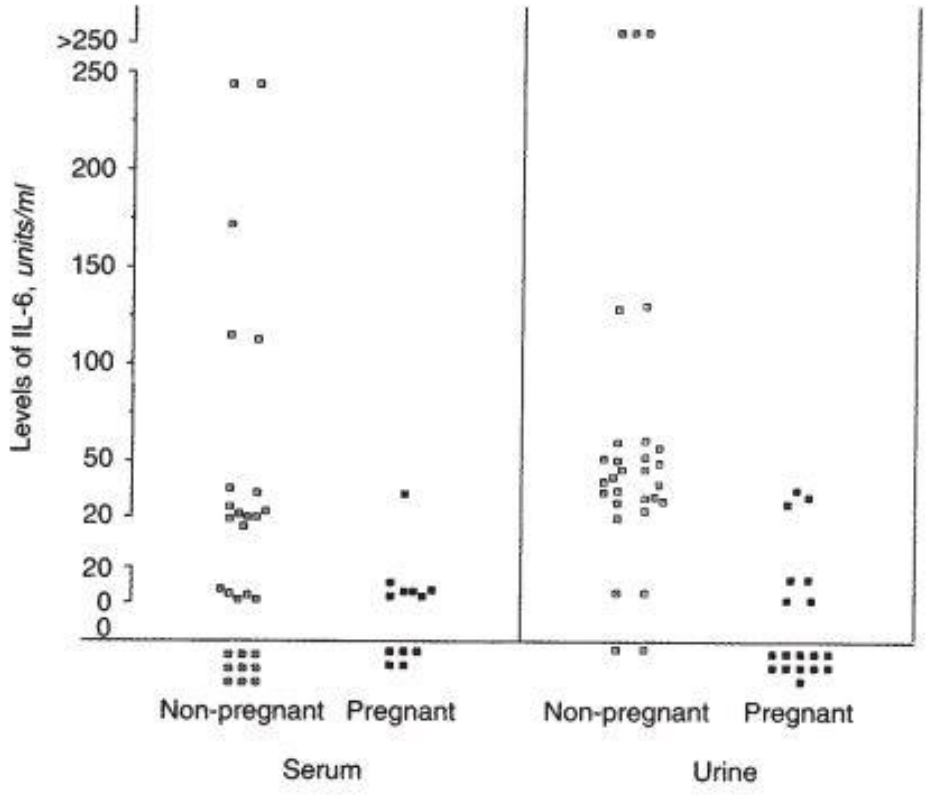


Figure 2. Urine and serum IL-6 activity in non-pregnant and pregnant women at the time of diagnosis of acute pyelonephritis. Adapted from Suppressed antibody and interleukin-6 responses to acute pyelonephritis in pregnancy. Petersson et al. 1994.(15)

When the levels of IL-6 in urine and serum were compared between pregnant and non-pregnant women, it was found that pregnant women had reduced levels of IL-6 to gram negative UTI which increases the risk of urinary tract infection in pregnant women (15).

MICROBIOLOGY

Urinary tract infection is most commonly caused by E.coli followed by Klebsiella in pregnant and non-pregnant women. Hill et al in 2005, studied pregnant women with pyelonephritis and found that the predominant uropathogen was E.coli with 83%, followed by Gram positive organisms like Group B Streptococcus which was 11.6%, followed by Klebsiella and Enterobacter which was 3.5% and Proteus which was 2.2% (16). Various studies looking at microbiology of urinary tract infection in pregnancy are summarized below.

TABLE 3: UROPATHOGENIC BACTERIA ISOLATED ACROSS LITERATURE

Study	Organism isolated
Hill et al (2005)(16) N= 32,282 440 patients developed antepartum pyelonephritis.	- E.coli- 83% - Gram positive cocci (GPC)- 11.6% - Klebsiella- Enterobacter- 3.5% - Proteus- 2.2%
Wing et al (2014) (6)	- E.coli- 82.5% - Streptococcus species- 21.4%

N= 2894 cases of antepartum pyelonephritis.	- Klebsiella pneumonia- 7.6% - Staphylococcus species- 6.5% - Proteus mirabilis- 4.9% - Enterococcus species- 5.7%
Sabharwal et al (2012) (7) N= 250 pregnant women.	- E.coli- 63.3% - Klebsiella- 8.3% - Pseudomonas- 1.7% - Proteus- 3.4% - Coagulase Negative Staphylococci (CONS)- 15% - Staphylococcus aureus- 8.3%
Rizvi et al (2011)(8) N= 8379 pregnant women.	- E. coli- 41.9% - Klebsiella pneumonia- 21.7% - Citrobacter species- 7.34% - Proteus mirabilis and Proteus vulgaris- 6.29% - Pseudomonas species- 3.4% - Staphylococcus saprophyticus and S.epidermidis- 6.4% - Staphylococcus aureus- 5.9% - Enterococcus faecalis- 3.4% - Streptococcus species- 3.4%

RISING PREVALENCE OF ANTIMICROBIAL RESISTANCE

Several studies have looked at the rising prevalence of antimicrobial resistance among urinary tract infection. Schito et al studied 4264 healthy women with symptoms of uncomplicated lower urinary tract infection. 3081 patients had significant growth of more than 100,000 colony forming units/ml of urine in the culture (17). E.coli was the most common pathogen isolated with 76.7% followed by Staphylococcus saprophyticus which was 3.6%, Klebsiella pneumoniae which was 3.5%, and Proteus mirabilis which was 3.4%. Other Enterobacteriaceae such as Serratia, Enterobacter, Citrobacter, Morganella, Pantoea, Salmonella, and Hafnia were only 2.9%. Schito et al looked at antimicrobial resistance pattern in strains of E.coli isolated from urinary tract infection (17). Ampicillin resistance was the most prevalent with 48.3 % of the E.coli strains being resistant to the same. This was followed by 29.4 % of the E.coli strains being resistant to Sulfamethoxazole/ Trimethoprim and 18.4% being resistant to Nalidixic acid (17). This study also looked at antimicrobial susceptibility pattern for Klebsiella, Proteus and Staphylococcus saprophyticus. 99% of the Klebsiella pneumoniae were resistant to Ampicillin followed by 37.4 % resistant to Nitrofurantoin, 23.3% resistant to Sulfamethoxazole/ Trimethoprim and 17.8 % being resistant to Nalidixic acid. The antimicrobial susceptibility pattern for Proteus showed 42.3% resistant to Nitrofurantoin, 37.5% resistant to Sulfamethoxazole/ Trimethoprim, 32.7 % resistant to Ampicillin, and 21.2% resistant to Nalidixic acid. 36.4 % of the Staphylococcus saprophyticus were resistant to Ampicillin followed by 10.4 % resistance to Sulfamethoxazole/ Trimethoprim.

Another study done in Aligarh by Rizvi et al looked at 8379 urine samples collected during the five year study period (8). Of these, 4290 (51.2 %) showed significant growth in urine culture. The uropathogen most commonly isolated were E.coli in 41.9%, followed by Klebsiella pneumoniae, Citrobacter, Staphylococcal species and Enterococcus faecalis. The antimicrobial susceptibility pattern were studied (8). Among the Enterobacteriaceae, Ciprofloxacin resistance was 64.5%, Cefotaxime resistance was 51.2%, Nitrofurantoin resistance was 40%, Amikacin resistance was 19%, and Cefoperazone- sulbactum resistance was 7.8%. This showed high rates of resistance to Ciprofloxacin and Nitrofurantoin. Around 34 % of the Staphylococcus species were methicillin resistant. However, there was no resistance to Vancomycin among the Staphylococcal species.

These studies showed that there is increase in urinary tract infections with ESBL producing uropathogen with significantly higher rate of resistance to beta-lactam group of antibiotics and Fluoroquinolones. Fluoroquinolones are contraindicated in pregnancy. This study also showed high rates of resistance to Nitrofurantoin (8).

CLINICAL PRESENTATION

Pregnant women can have bacteriuria which can be asymptomatic or symptomatic.

ASYMPTOMATIC BACTERIURIA IN PREGNANCY

IDSA 2005 guidelines, defined asymptomatic bacteriuria. It was defined as two consecutive voided urine specimens with isolation of the same bacterial isolate in ≥ 100,000 colony forming units/ml in case of mid-stream voided urine sample or ≥ 100

colony forming units/ml in case of catheterized urine specimen (3). IDSA recommends screening of pregnant women for bacteriuria by urine culture at least once in early pregnancy which is before 16 weeks following which they showed be treated with appropriate antimicrobial therapy for 3 to 7 days in case of positive results. Periodic screening showed be done to look for recurrent bacteriuria in pregnancy and prophylactic antibiotics might be required (3).

SYMPTOMATIC BACTERIURIA IN PREGNANCY

Symptomatic bacteriuria can be further divided into the following types.

- ACUTE CYSTITIS
- ACUTE PYELONEPHRITIS

Acute cystitis occurs secondary to infection and inflammation of the bladder. The patient presents with complains of dysuria, urinary urgency and frequency in the absence of fever and chills. As the pregnant women is symptomatic for the same and seeks treatment and the load of infection is mild, this is usually not associated with adverse outcomes. However, they are prone of recurrent bacteriuria (12,18). The incidence of cystitis during pregnancy is around 1 to 2% (5).

Acute pyelonephritis occurs due to infection of the upper urinary tract and kidneys. These patients present with fever more than 100.4 F with flank pain, vomiting with nausea and costovertebral tenderness. The incidence of pyelonephritis among pregnancy is 0.5 to 2% (6,16). In view of severe infection, it is associated with adverse maternal and fetal

outcomes. Adverse maternal outcomes that occur include anemia, acute kidney injury, sepsis, acute respiratory distress syndrome. Adverse fetal outcomes that occur include preterm birth and low birth weight (12).

SPECIMEN COLLECTION

There are three techniques for collection of urine for culture

1. Mid-stream voided sample
2. Mid-stream clean catch voided sample.
3. Urethral catheter sample
4. Suprapubic aspiration.

Proper specimen with as minimal contamination is required for appropriate diagnosis. Suprapubic aspiration is not feasible for pregnant women in view of the distended uterus and risk of trauma to the fetus. Urethral catheter sample in a sterile technique will help getting an accurate diagnosis. However, this technique is cumbersome and there is risk of introducing infection. Mid-stream sample is easy to collect but there is high risk of contamination. Mid-stream voided sample is collected by spreading the labia and collecting a midstream urine. Mid-stream clean catch voided sample differs from mid-stream voided sample as it is collected after local cleansing of the urethral meatus and surrounding mucosa and then collecting the second portion of urine after discarding the first portion. Study done by Schneeberger C et al in 2013, showed that the rates of contamination between midstream voided sample and midstream clean catch sample were similar(19).

CRITERIA FOR DIAGNOSIS OF URINARY TRACT INFECTION

ASYMPTOMATIC BACTERIURIA

IDSA 2005 guidelines defines asymptomatic bacteriuria as

> -"2 consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts of more than 10^5 colony forming units (CFU)/mL. "
>
> OR
>
> -"A single catheterized urine specimen with 1 bacterial species isolated in a quantitative count of 10^2 CFU/mL identifies bacteriuria in women." (3)

The original criterion for diagnosing asymptomatic bacteriuria which is more than 100,000 CFU of bacteria/ml on two consecutive clean catch samples is cumbersome and not feasible in many situations due to financial constraints. The detection of more than 100,000 CFU of bacterial/ ml in a single voided midstream urine is accepted as an adequate and more practical alternative, although there is only an 80% probability the woman has true bacteriuria. This probability increases to 95% if two or more consecutive cultures show significant growth (20,21).

ACUTE CYSTITIS.

Criteria for diagnosis of acute cystitis include

- Symptomatic urinary tract infection in the form of dysuria, increased frequency, urgency, lower abdominal pain with
- Urine culture showing more than 100,000 CFU/ml of organism in a mid-stream clean catch urine or more than 100 CFU/ml in case of catheterized urine sample.

ACUTE PYELONEPHRITIS

Criteria for diagnosis include

- Symptomatic urinary tract infection with features of upper urinary tract infection in the form of fever with chills, lower back pain, renal angle tenderness with or without symptoms of lower urinary tract infection.
- Urine culture showing more than 100,000 CFU/ml of organism in a mid-stream clean catch urine or more than 100 CFU/ml in case of catheterized urine sample.

DEFINITIONS

Primigravida refers to a women who is pregnant for the first time (22).

Multigravida refers to women who has been pregnant more than 2 times(23).

Grand multigravida refers to a women who has had 5 or more deliveries (24).

Elderly gravida refers to a women who becomes pregnant at an age of 35 years or more (25).

Teenage pregnancy is defined as pregnancy in a women of 19 years of age or less (26).

Singleton pregnancy refers to single live intrauterine fetus (26)

Multifetal pregnancy refers to 2 or more live intrauterine fetuses (26)

Modified kuppuswamy scale, 2016 was used for calculating socioeconomic status of the participants (27). The basis of scoring and classification is shown in the table below.

Table 3: Scoring for modified Kuppuswamy's socio-economic status scale, revised for 2016.

Education	**Score**
Professional or honors	7
Graduate or postgraduate	6
Intermediate or post-high school diploma	5
High School Certificate	4
Middle School certificate	3
Primary School certificate	2
Illiterate	1
Occupation	**Score**
Professional	10
Semi-Professional	6
Clerical, Shop Owner, Farmer	5
Skilled Worker	4
Semi-Skilled Worker	3
Unskilled Worker	2
Unemployed	1
Family income per month in Rupees (August 2016 current price index for industrial workers)	**Score**
≥ 42,876	12
21,438-42,875	10
16,078-21,437	6
10719-16,077	4
6,431-10,718	3
2,165-6,430	2
≤2164	1

Table 4: Kuppuswamy's classification of socioeconomic status.

Class	**Total Score**
Upper class	26-29
Upper middle class	16-25
Lower middle class	11-15
Upper lower class	5-10
Lower class	<5

Anemia

It is defined by Indian council of Medical Research, ICMR as per the following criteria.

Table 5: ICMR definition of anemia

DEGREE OF ANEMIA	HEMOGLOBIN CUT OFF
Mild	10 to 10.9 g/dl
Moderate	7-9.9
Severe	<7
Very Severe	<4

DEFINITION OF MATERNAL OUTCOMES

Placental abruption

Placental abruption is defined as the premature separation of the implanted placenta before the delivery of the fetus which is diagnosed based on clinical symptoms that include vaginal bleeding accompanied with severe abdominal pain, uterine tenderness, or tetanic contractions (28).

Gestational Hypertension

The diagnosis of gestational hypertension is made in women whose blood pressure reaches 140/90 mm Hg or greater for the first time after mid pregnancy, but in whom proteinuria is not identified(29)

Pre-eclampsia

Pre- eclampsia is defined as new onset hypertension after 20 weeks of gestation with the following criteria (30).

<table>
<tr><td>Blood pressure</td><td>Greater than or equal to 140 mmHg systolic or greater than or equal to 90 mm Hg diastolic on 2 occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure.
Greater than or equal to 160 mm Hg systolic or greater than or equal to 110 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy.</td></tr>
<tr><td colspan="2">And</td></tr>
<tr><td>Proteinuria</td><td>Greater than or equal to 300 mg per 24 hour urine collection (or this amount extrapolated from a timed collection)
OR
Protein/ creatinine ratio greater than or equal to 0.3.
Dipstick reading of 1+ (used only if other quantitative methods not available)</td></tr>
<tr><td colspan="2">Or in the absence of proteinuria, new onset hypertension with the new onset of any of the following.</td></tr>
</table>

Thrombocytopenia	Platelet count less than 100,000/ microliter.
Renal insufficiency	Serum creatinine concentrations greater than 1.1 mg/dl or a doubling of the serum creatinine concentrations in the absence of other renal disease
Impaired renal function	Elevated blood concentrations of liver transaminases to twice normal concentration
Pulmonary edema	
Cerebral or visual symptoms	

Severe Pre- eclampsia

Any of these findings makes the Pre- eclampsia severe-

- Systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensive therapy is initiated before this time).
- Thrombocytopenia (platelet count less than 100,000/ microliter).
- Impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnosis or both.

- Progressive renal insufficiency (serum creatinine concentration greater than 1.1 mg/dl or a doubling of the serum creatinine concentration in the absence of other renal disease).
- Pulmonary edema.
- New onset cerebral or visual disturbances.

Eclampsia

Eclampsia is defined as the presence of new onset grand mal seizures in a woman with pre eclampsia. Eclampsia can occur before, during or after labor (30).

Premature rupture of membranes (PROM)

Premature rupture of the fetal membranes (PROM) is defined as the rupture of the amniotic membranes with release of the amniotic fluid more than 1 hour prior to the onset of labor. PROM may be subdivided into term PROM (i.e. PROM after 37 weeks of gestation) and preterm PROM (PPROM, i.e. PROM prior to 37 weeks of gestation) (31).

Chorioamnionitis

Chorioamnionitis or intraamniotic infection is an acute inflammation of the membranes and chorion of the placenta, typically due to ascending polymicrobial bacterial infection in the setting of membrane rupture. Clinical symptoms include fever, uterine fundal

tenderness, maternal tachycardia (>100/min), fetal tachycardia (>160/min) and purulent or foul amniotic fluid (32).

Acute Pyelonephritis

Acute pyelonephritis is an infection of the renal pelvis and kidney that usually results from ascent of a bacterial pathogen up the ureters from the bladder to the kidneys, is associated with lower urinary tract symptoms (e.g., urinary frequency, urgency, dysuria) accompanied by fever, nausea, vomiting, or flank pain with examination showing tenderness to palpation of the costovertebral angle (33).

Operative Vaginal Delivery/ Instrumental Delivery

Operative vaginal delivery are accomplished by applying direct traction on the fetal skull with forceps, or by applying traction to the fetal scalp by means of a vacuum extractor(34) .

Cesarean Delivery

A cesarean birth, often called a C-section, is the delivery of the baby through incisions in the mother's abdomen and uterus (35).

DEFINITION OF FETAL OUTCOMES

Intrauterine Growth Restriction (IUGR)

IUGR is a fetus whose estimated weight is below the 10th percentile for its gestational age and whose abdominal circumference is below the 2.5th percentile for its gestational age (36).

Preterm delivery

Preterm is defined as babies born alive before 37 weeks of pregnancy are completed. There are sub-categories of preterm birth, based on gestational age:

- Extremely preterm (<28 weeks)
- Very preterm (28 to <32 weeks)
- Moderate to late preterm (32 to <37 weeks) (37).

Low birth weight

Low birth weight has been defined by the World Health Organization (WHO) as weight at birth of less than 2,500 grams (5.5 pounds) (38).

Very low birth weight is less than 1,500 g (up to and including 1,499 g) (38).

Extremely low birth weight is less than 1,000 g (up to and including 999 g) (38).

Still birth

Stillbirth is a fetal death that occurs during pregnancy at 22 weeks or greater gestation or at weight greater than or equal to500g (39).

Birth Asphyxia

AAP/ACOG criteria (40).

1. Arterial cord pH < 7.0
2. Apgar score of 3 or less for greater than 5 minutes
3. Evidence of altered neurological status (seizures, obtundation, etc.)
4. Multisystem organ injury or failure

RATIONALE FOR TREATMENT OF URINARY TRACT INFECTION IN PREGNANCY

As mentioned earlier, the incidence of bacteriuria is similar between pregnant and non-pregnant women. However, pregnant women are at higher risk for symptomatic urinary tract infection and recurrent bacteriuria (1). Several studies have shown that treatment of asymptomatic bacteriuria reduces the incidence of symptomatic urinary tract infection and improves outcome. This was shown in a meta-analysis which was published in Cochrane Database Systematic review in 2015. It looked at randomized trials which involved pregnant women who were diagnosed with asymptomatic bacteriuria on antenatal checkup

and compared antibiotic treatment versus no treatment or placebo in them. There was a total of 14 studies which involved 2000 women which showed that antibiotic therapy reduced the incidence of pyelonephritis (average risk ratio (RR) 0.23, 95% confidence interval (CI) 0.13 to 0.41), reduced the incidence of low birth weight infants (average RR 0.64, 95% CI 0.45 to 0.93) and preterm birth (RR 0.27, 95% CI 0.11 to 0.62), and there was reduction in persistent bacteriuria (average RR 0.30, 95% CI 0.18 to 0.53). This meta-analysis showed that antibiotic treatment in case of asymptomatic bacteriuria was beneficial in reducing the risk of pyelonephritis. On the other hand, the quality of evidence was poor and the conclusions have to be interpreted with caution(1).

Study done in Soroka University Medical Center, Israel, looked at 199,093 singleton deliveries which occurred in this hospital between 1988 and 2007. Pregnant women with asymptomatic bacteriuria were excluded. The study compared pregnant women with culture proven symptomatic urinary tract infection with pregnant women without urinary tract infection. Out of the 199,093 deliveries, 4742 which is 2.3% had symptomatic UTI. Pregnant women with symptomatic UTI had a higher incidence of preterm delivery, lower birth weight, recurrent abortions, intrauterine growth restrictions, premature rupture of membranes, chorioamnionitis, and caesarean delivery. Renal abnormalities such as pyelonephritis, hydroureteronephrosis, renal nephrolithiasis and renal abscess were more common in pregnant women with UTI. Assessment of fetal and neonatal outcome also revealed that pregnant women with UTI had infants with lower APGAR score at 1 min but similar APGAR score at 5 min and perinatal mortality in the two arms were also comparable (41). All these studies reveal that treatment of asymptomatic bacteriuria and

symptomatic urinary tract infection during pregnancy results in better maternal and fetal outcomes.

MANAGEMENT OF URINARY TRACT INFECTIONS DURING PREGNANCY

Pregnant women with symptoms of urinary tract infection requires treatment in view of the adverse outcomes associated with it as mentioned above. They can be treated with oral or IV antibiotics based on the severity of symptoms (42). In case of mild symptoms, oral antibiotics usually suffice. In case of signs of sepsis or systemic symptoms, the pregnant women will require admission for intravenous antibiotics. In such patients, ultrasound abdomen is required to look for renal abscess and hydroureteronephrosis. Antimicrobial susceptibility reports need to be followed by and antibiotics appropriately tailored for the same.

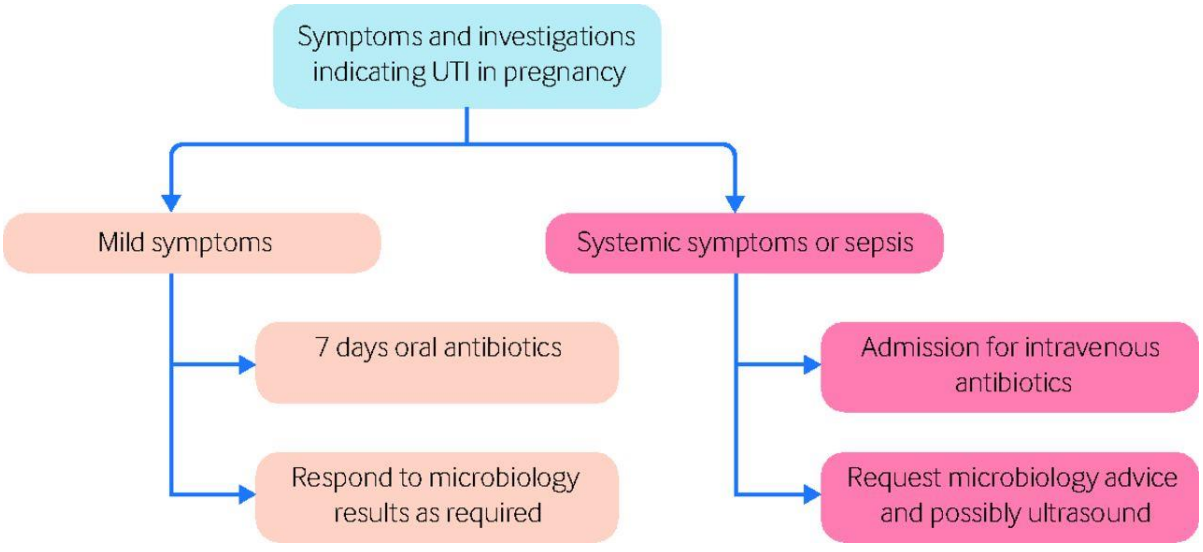


Figure 3. Suggested approach to the management of urinary tract infection (UTI) in pregnancy in women who have no signs of fetal compromise. Adapted from A likely urinary tract infection in a pregnant woman. Johnston et al. BMJ 2017.(42)

Based on the pathogenic organisms and trimester of pregnancies, a variety of antimicrobial agents are available for treatment of urinary tract infection. Treatment is challenging in pregnant women in view of teratogenicity of certain antimicrobial agents on the fetus and in view of the rising prevalence of antimicrobial resistance among the pathogenic organisms. The figure below looks at commonly used antimicrobial agents and fetal toxicity.

Antimicrobials in pregnancy

Drug	Fetal Toxicity	Comments	Prior FDA Category
Penicillins			
Penicillin G	Low risk	Commonly used	B
Amoxicillin	Low risk	Commonly used	B
Ampicillin	Low risk	Commonly used	B
Cephalosporins			
Cephalexin	Low risk	1st generation; commonly used	B
Cefuroxime	Low risk	2nd generation; commonly used	B
Ceftriaxone	Low risk	3rd generation; commonly used	B
Ceftazidime	Low risk (limited data)	3rd generation with antipseudomonal coverage	B
Cefepime	Low risk (limited data)	4th generation with antipseudomonal coverage	B
Monobactams			
Aztreonam	Low risk (limited data)	Limited data; consider ID consultation	B
Carbapenems			
Imipenem	Very limited data	Limited data; must be administered with cilastatin; consider ID consultation	C
Meropenem	Very limited data	Limited data; consider ID consultation	B
Lincosamides			
Clindamycin	Low risk	Commonly used; useful in penicillin-allergic patients	B
Macrolides			
Azithromycin	Low risk	Commonly used	B
Erythromycin	Low risk	More gastrointestinal side effects than azithromycin	
Nitrofurans			
Nitrofurantoin	Controversial teratogenic risk; risk of hemolytic anemia in G6PD deficiency during third trimester	Commonly used; use for only for lower UTIs	B
Phosphonics			
Fosfomycin	Low risk (limited data)	Use for only for lower UTIs	B
Sulfonamides			
Sulfadiazine	Risk of antifolate teratogenesis; risk of hyperbilirubinemia in third trimester	Avoid if alternatives available	C
Trimethoprim-sulfamethoxazole	Risk of antifolate teratogenesis	Avoid in pregnancy	C
Glycopeptides			
Vancomycin	Very limited data	Limited data; consider ID consultation	B

(continued on next page)

Drug	Fetal Toxicity	Comments	Prior FDA Category
Oxazolidinones			
Linezolid	Only case reports available	Limited data; consider ID consultation	C
Lipopeptides			
Daptomycin	Only case reports available	Limited data; consider ID consultation	B
Aminoglycosides			
Gentamycin	Potential risks of ototoxicity and nephrotoxicity	Commonly used; useful for pyelonephritis	C
Fluoroquinolones			
Ciprofloxacin	Theoretic risk of arthropathy	Avoid in pregnancy	C
Tetracyclines			
Tetracycline	Risk of teratogenicity and discoloration of teeth/bones	Avoid in pregnancy	D
Doxycycline	—	Avoid in pregnancy	D

Abbreviations: G6PD, glucose-6-phosphate dehydrogenase; ID, infectious disease.

Figure 4. Antimicrobials in pregnancy. Adapted from Urinary Tract Infection and Bacteriuria in Pregnancy. Glaser et al. Urology clinics of North America. 2015(12).

This shows that a wide variety of antimicrobial agents are available for the treatment of UTI in pregnancy but the options are limited when it comes to infections with resistant organisms as data for newer antibiotics are limited.

MATERIALS &METHODS

SETTING

This study was carried out in Christian Medical College (CMC), Vellore, which is a 2700-bedded tertiary care teaching hospital in South India. The hospital serves the population of Tamil Nadu and the neighboring state of Andhra Pradesh, besides being a referral center for patients from other parts of the country and the Indian subcontinent.

Patients were recruited from June 2017 to June 2018 after obtaining approval from the institutional research board (IRB No. 10627).

STUDY DESIGN

This was a cross-sectional study. Pregnant women who delivered in CMC and CMC allied hospitals, with at least 3 visits to the OPD prior to delivery were included.

PARTICIPANTS

Pregnant women with symptomatic urinary tract infection with culture confirmed infection were recruited as cases. Controls were pregnant women without symptomatic urinary tract infection who delivered in CMC or CMC allied hospitals.

BASELINE ASSESSMENT FOR THE PREGNANT WOMEN:

All pregnant women who visit CMC, undergo regular antenatal check up with the following tests

Clinical parameters

a. Heart rate of mother
b. Blood pressure of mother
c. Size of uterus
d. Fetal movements
e. Fetal heart sound

Laboratory parameters

a. Haemoglobin
b. Urine routine
c. Urine culture

d. OGTT

e. VDRL

f. Fetal ultrasound

g. Urine albumin.

INCLUSION CRITERIA:

Inclusion criteria for this study-

- Pregnant women more than 18 years of age.
- Should have received antenatal care from CMC (3 visits before labour).
- Should have delivered in CMC labour room.
- Should give informed consent.

EXCLUSION CRITERIA:

Exclusion criteria for prospective arm of this study.

- Participants who do not give informed consent.
- Participants who are not booked for antenatal care in CMC.

STUDY PROCEDURE:

In this cross sectional study, pregnant women who deliver in CMC, will be assessed for history of symptomatic UTI with positive urine culture and will be compared with pregnant women without UTI to assess the adverse maternal and fetal outcomes that occur secondary to UTI. The participants were recruited from July 2017 to August 2018 from CMC labour room after taking informed consent. They were then interviewed during their stay in hospital for risk factors that predispose to UTI. The fetal and maternal outcomes as pre-

specified were collected from the patients chart and the data entry forms were filled. The data from Clinical microbiology on urine and blood culture characteristics were collected for assessing the antimicrobial susceptibility pattern.

PATIENT RECRUITMENT AND ASSESSMENT:

Pregnant women who delivered in CMC labor room were recruited. Cases were pregnant women who delivered in CMC with past history of urinary tract infection during the antenatal period with urine culture showing more than 100,000 CFU/ml of pathogenic organisms in mid-stream clean catch urine specimen or more than 100 CFU/ml in catheter sample.

Pregnant women without symptomatic urinary tract infection who delivered in CMC labor room was recruited as controls.

The participants were recruited after delivery in CMC when they were visited and informed consent was taken following which questionnaire was administered to them.

OUTCOMES ASSESSED
PRIMARY OUTCOME:

To determine the maternal and foetal outcomes secondary to symptomatic urinary tract infection in pregnancy.

SECONDARY OUTCOMES:

- To determine the risk factors associated with Urinary tract infection in pregnancy.
- To identify the organisms causing UTI.
- To identify the antimicrobial susceptibility pattern of the organisms.

SAMPLE SIZE

The required sample size to find the maternal and neonatal outcomes due to UTI during pregnancy was found to be about 200 UTI and 400 non UTI subjects with 80% power and 5% level of significance with an anticipated proportion of 8% preterm delivery among UTI women which was taken from the article written by Efrat Mazor-dray et al which was published in February 2009 (41).

Formula:

$$n_1 = m' = \frac{\left\{Z_\alpha \sqrt{(r+1)\bar{P}\bar{Q}} + Z_\beta \sqrt{r P_1 Q_1 + P_2 Q_2}\right\}^2}{r\delta^2} \qquad n_2 = m' \times r$$

$$N = n_1 + n_2$$

$$\delta = P_2 - P_1\,; \quad \bar{P} = \frac{P_1 + rP_2}{r+1}\,; \quad \bar{Q} = 1 - \bar{P}$$

Where,

P_1 : Proportion in the first group

P_2 : Proportion in the second group

δ : Difference in the two proportions

r : Allocation ratio

α : Significance level

$1-\beta$: Power

Reference for above formula: Sahai H, Kurshid A. Formulae and tables for the determination of sample size and power in clinical trials for testing differences in proportions for the two sample design: a review. Statistics in Medicine, 1996; 15: 1-21.

Epidemiology Methods - Unmatched Cross sectional Studies - Equal Allocation - Hypothesis testing of the odds ratio

Probability of exposure in control group	0.08
Anticipated odds ratio	2
Probability of exposure in case group	0.1481
Power (1- beta) %	80
Alpha error (%)	5
1 or 2 sided	2
Required sample size in each of the case && control groups	341

Hence, the calculated sample size was 341 in each arm.

STATISTICAL ANALYSIS:

Data entry was done using EPIDATA Software 3.1. Statistical analysis was done SPSS version 24. The quantitative variables were birth weight of the baby, gestational age of the mother, age of the mother. These variables were expressed in terms of mean with standard deviation (SD) or median with Interquartile range (IQR) based on the distribution of the variables in each group. The comparison of the quantitative variables were done using independent t-test or Wilcoxon rank sum test depending on the distribution.

The categorical variables like preterm delivery, IUGR, pre-eclampsia, etc., were expressed as frequencies across the UTI and non UTI subjects. Comparison of these variables across the groups were done using Fisher's Exact test.

All significant variables in the above analysis were analysed using Logistic regression and P value < 0.05 was considered as statistical significance. Hosmer Lemeshow statistic were reported to assess the goodness of fit of the final model.

INSTITUTIONAL REVIEW BOARD AND ETHICS COMMITTEE CLEARANCE:

The study design and methods were approved by the institutional review board (blue) and ethics committee of Christian Medical College, Vellore (IRB Min. No. 10627, dated 04.04.2017). A copy of the IRB approval statement can be found in Annexure.

FUNDING OF THE STUDY:

This study was funded by fluid research grant number 22Z404 of Christian Medical College, Vellore.

STUDY FLOW DIAGRAM:

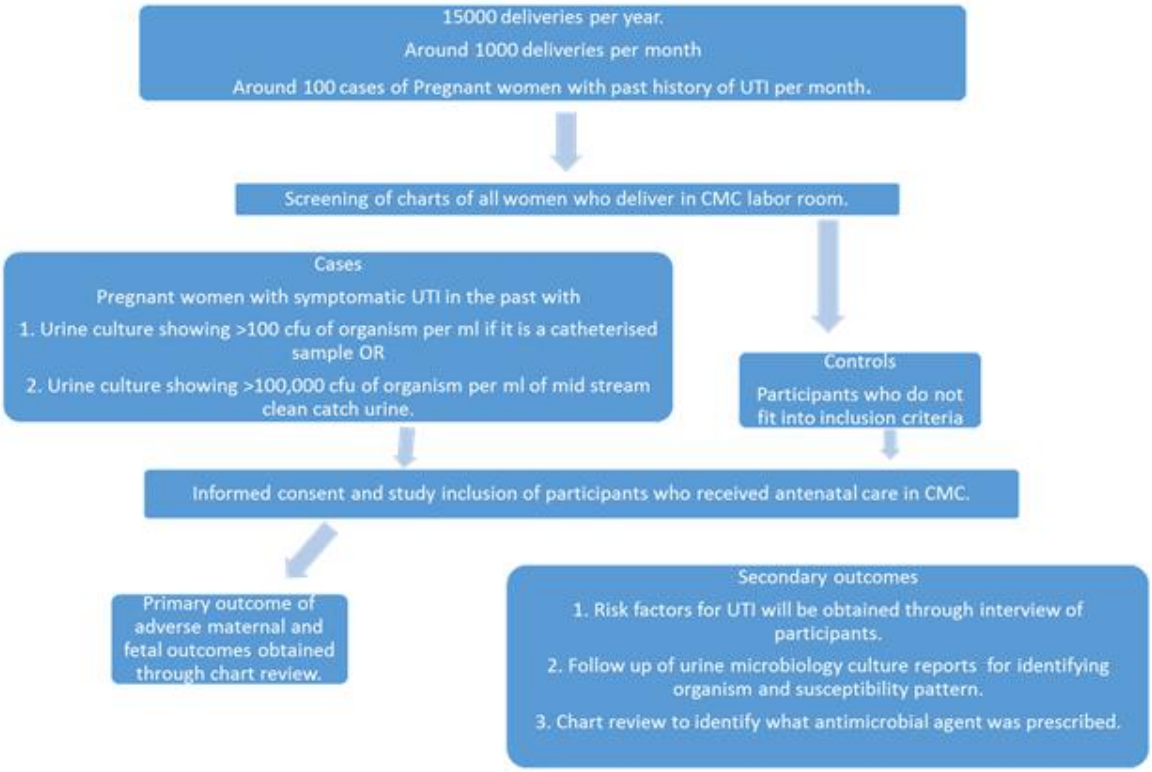
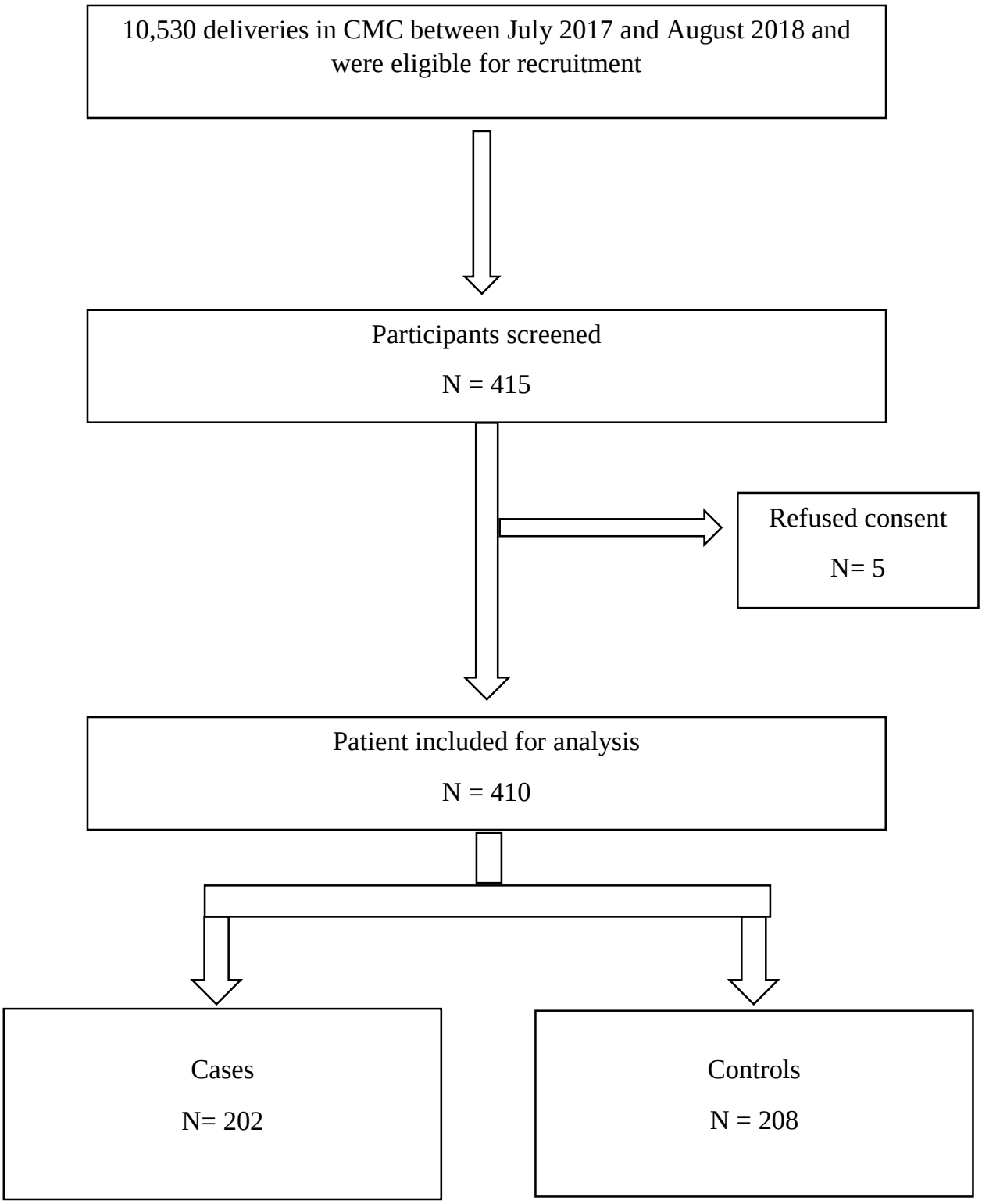


FIGURE 11: Study flow diagram

RESULTS

This cross sectional study was done from July 2017 through August 2018. During this period 415 patients were recruited. Five patients were excluded, as they refused to provide consent. Thus, four hundred and ten patients (N= 410) patients were included in the final analysis (Figure 12).

FIGURE 12: STROBE Diagram



BASELINE CHARACTERISTICS OF CASES AND CONTROLS

410 patients were recruited for the study. Of the 410 patients, 202 were cases and 208 were controls. Mean age of the study population was 26.44, with median of 26 (IQR: 18 – 45) years. It composed mainly of women from Tamil Nadu and Andhra Pradesh as only women for were booked for the antenatal care in this institution were included.

Table 6: Baseline characteristics of the cases and controls (N = 410)

Sex	Female	Cases 100%	Controls 100%
Mean Age (Mean +/- SD)	26.44	28.65 +/- 4.20	26.05 +/- 4.20
Parity	Primigravida 216 (52.6%) Multigravida 187 (45.6%) Grand multigravida 7 (1.7%)	Cases- 116 (57.4%) Cases- 81 (40.1%) Cases- 5 (2.5%)	Controls- 100 (48.1%) Controls- 106 (51%) Controls- 2 (1%)
Singleton pregnancy Multifetal pregnancy	401 (97.8%) 9 (2.2%)	Cases-194 (96%) Cases- 8 (4%)	Controls- 207 (99.5%) Control- 1 (0.5%)

Fertility treatment Yes No	 22 (5.4%) 388 (94.6%)	 Cases- 13 (6.4%) Cases- 189 (93.6%)	 Controls- 9 (4.3%) Controls- 199 (95.7%)
Number of abortions 1 2 3	 55 (13.4%) 20 (4.8%) 4 (1%)	 Cases- 26 (12.9%) Cases- 13 (6.4%) Cases- 2 (1%)	 Control- 29 (13.9%) Controls- 7 (3.4%) Controls- 2 (1%)
Number of recurrent abortions	Total= 24 (5%)	Cases- 15	Controls- 9
Educational status Primary school Middle school High school Intermediate or post high school Graduate or post graduate	 1 (0.2%) 57 (13.9%) 129 (31.5%) 73 (17.8%) 147 (35.9%)	 Case- 0 Case- 36 (17.8%) Case- 64 (31.7%) Case- 56 (27.7%) Case- 46 (22.8%)	 Control- 1 (0.5%) Control- 21 (10.1%) Control- 65 (31.3%) Control- 17 (8.2%) Control- 101 (48.6%)

Professional or honors	3 (0.7%)	Case- 0	Control- 3 (1.4%)
Occupation			
Unemployed	6 (1.4%)	Case- 6 (2.9%)	Control- 0
Unskilled	34 (8.2%)	Case- 7 (3.5%)	Control- 27 (12.98%)
Semiskilled	11 (3.7%)	Case- 2 (0.99%)	Control- 9 (4.32%)
Skilled	27 (6.6%)	Case- 16 (7.9%)	Control- 11 (5.3%)
Clerical/ Farmer/ Shop owner	155 (37.8%)	Case- 93 (46%)	Control- 62 (29.8%)
Semi professional	94 (22.9%)	Case-47 (23.3%)	Control- 47 (22.6%)
Professional	83 (20.2%)	Case- 31 (15.3%)	Control-52 (25%)
Family monthly income (Rs)			
0 – 2091	1 (0.2%)	Case- 1 (0.5%)	Control- 0
2092 – 6213	5 (1.2 %)	Case- 5 (2.5%)	Control- 0
6214 – 10356	71 (17.3%)	Case- 29 (14.4%)	Control- 42 (20.2%)
10357 – 15535	160 (39%)	Case- 72 (35.64%)	Control- 89 (42.8%)
15536- 20714			

20715- 41429 > 41430	102 (24.9%) 54 (13.2%) 17 (4.1%)	Case- 57 (28.2%) Case- 23 (11.4%) Case- 16 (7.9%)	Control- 45 (21.6%) Control- 31 (14.9%) Control- 1 (0.5%)
Modified kuppuswamy SES score Upper lower Lower middle Upper middle Upper	55 (13.4%) 174 (42.4%) 135 (2.9%) 46 (11.2%)	Case- 20 (9.9%) Case- 100 (49.5%) Case- 62 (30.7%) Case- 20 (9.9%)	Control- 35 (16.8%) Control- 74 (35.6%) Control- 73 (35.1%) Control- 26 (12.5%)
Genitourinary abnormality	15 (3.6%)	Cases- 9 (4.5%)	Controls- 6 (2.9%)
Past history of catheterization	34 (8.3%)	Cases- 24 (11.9%)	Control- 10 (4.8%)
Past history of UTI	4 (0.97%)	Cases- 4 (2%)	Controls- 0
Gestational diabetes mellitus	102 (24.9%)	Cases- 49 (24.3%)	Controls- 53 (25.5%)

Pregestational diabetes mellitus	6 (1.5%)	Cases- 5 (2.5%)	Controls- 1 (0.5%)
Chronic hypertension	8 (2%)	Cases- 3 (1.5%)	Controls- 5 (2.4%)

PARITY OF PREGNANCY

53.2% of the women were primigravida, 46.3% of the women were multigravida and 0.5% were grand multipara. Among the cases 57.4 % were primigravida and 40.1 % were multigravida. Among the controls, 48.1 % were primigravida and 51 % were multigravida.

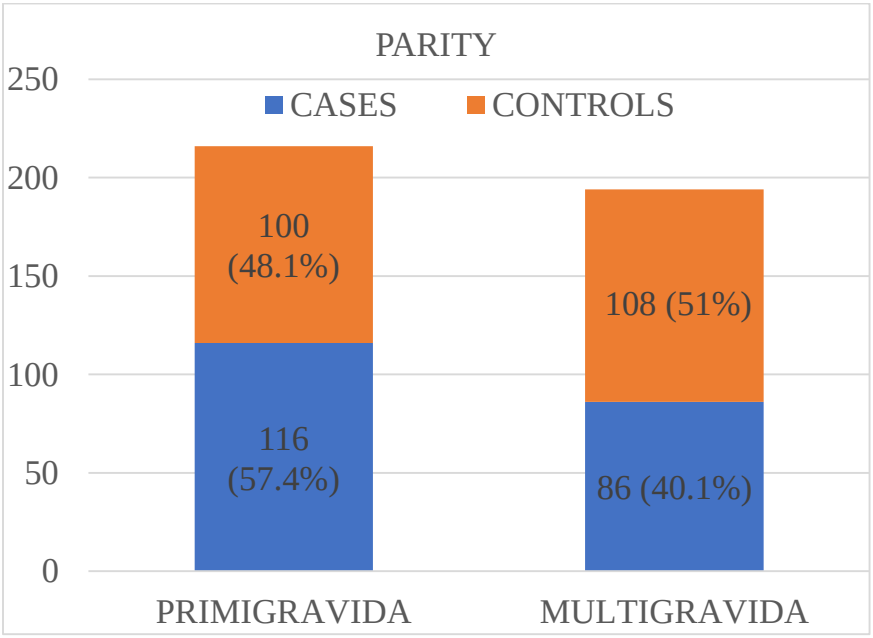


Figure 5: Distribution of parity among cases and controls

SINGLETON VERSUS MULTIFETAL PREGNANCY

Among the participants studied, 97.8% had singleton pregnancy and 2.2% had multifetal pregnancy which has been represented in the pie chart.

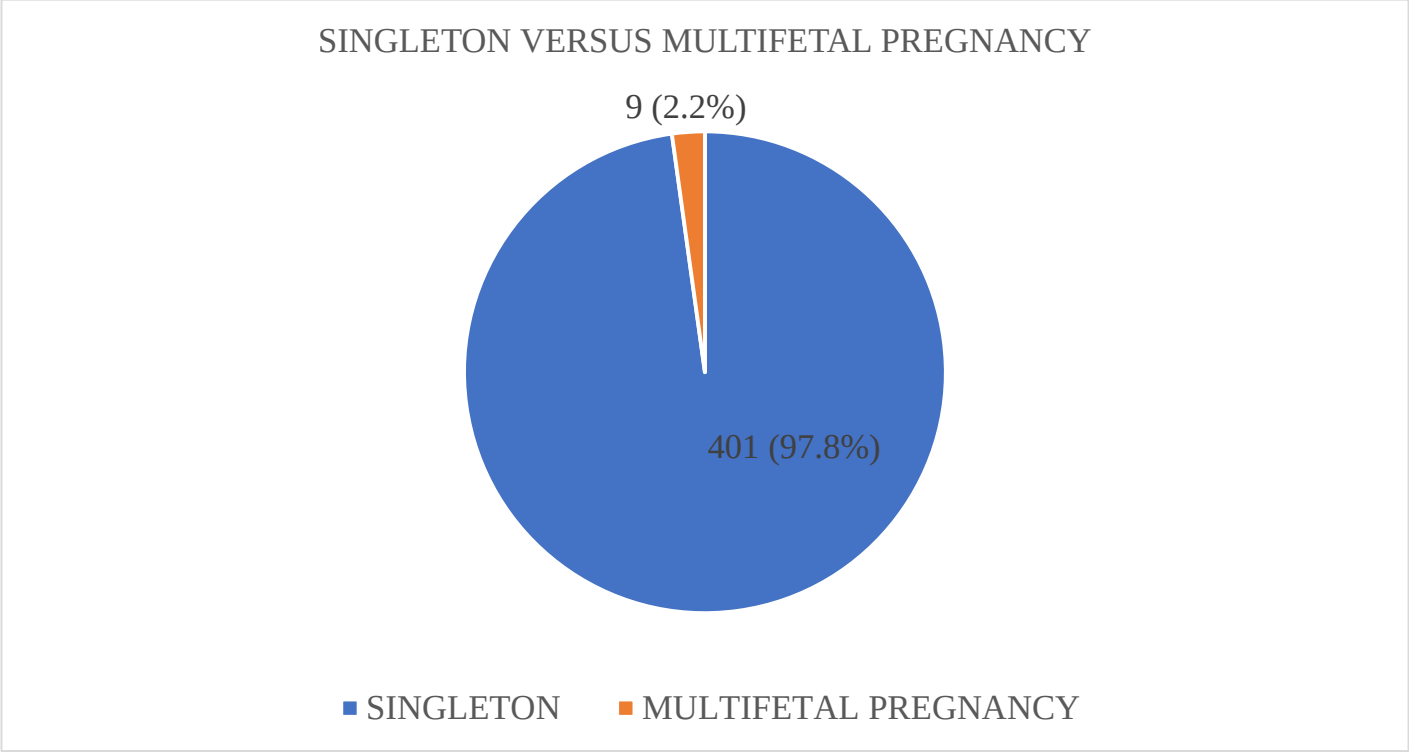


Figure 6: Singleton versus multifetal pregnancy.

EDUCATIONAL STATUS

Majority of the participants have received some form of education with 13.9 % completing middle school education, 31.5 % completing high school education, 17.8% completing Intermediate or post high school diploma, and 35.9% completing graduate courses.

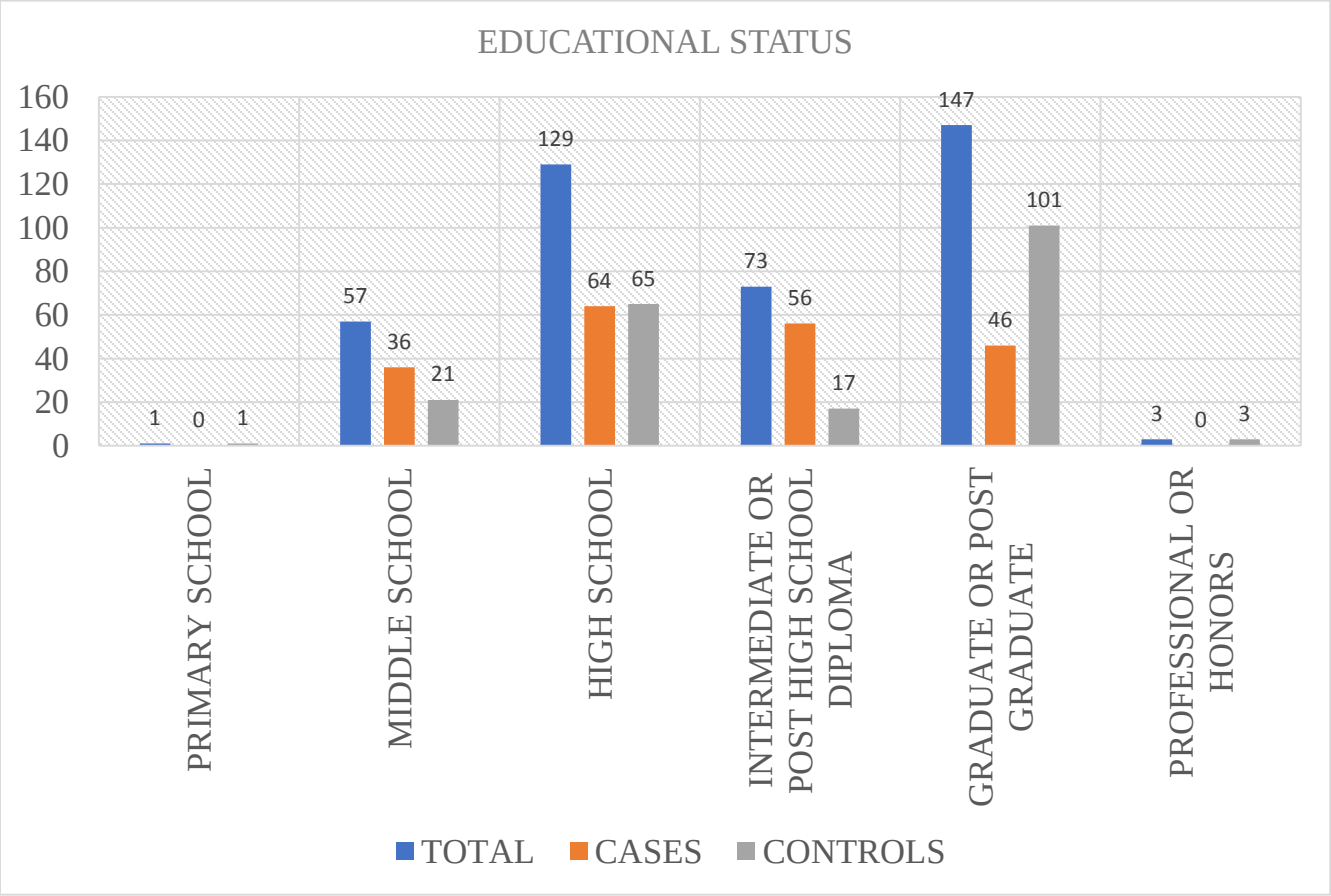


Figure 7: Educational status

OCCUPATIONAL STATUS

Majority of the participants have employed with 37.8 % working in a clerical/ farming/ shop owner profession, 22.9 % employed in semiprofessional job and 20.2% employed in a professional job. 1.4% were unemployed and 8.2% had an unskilled profession.

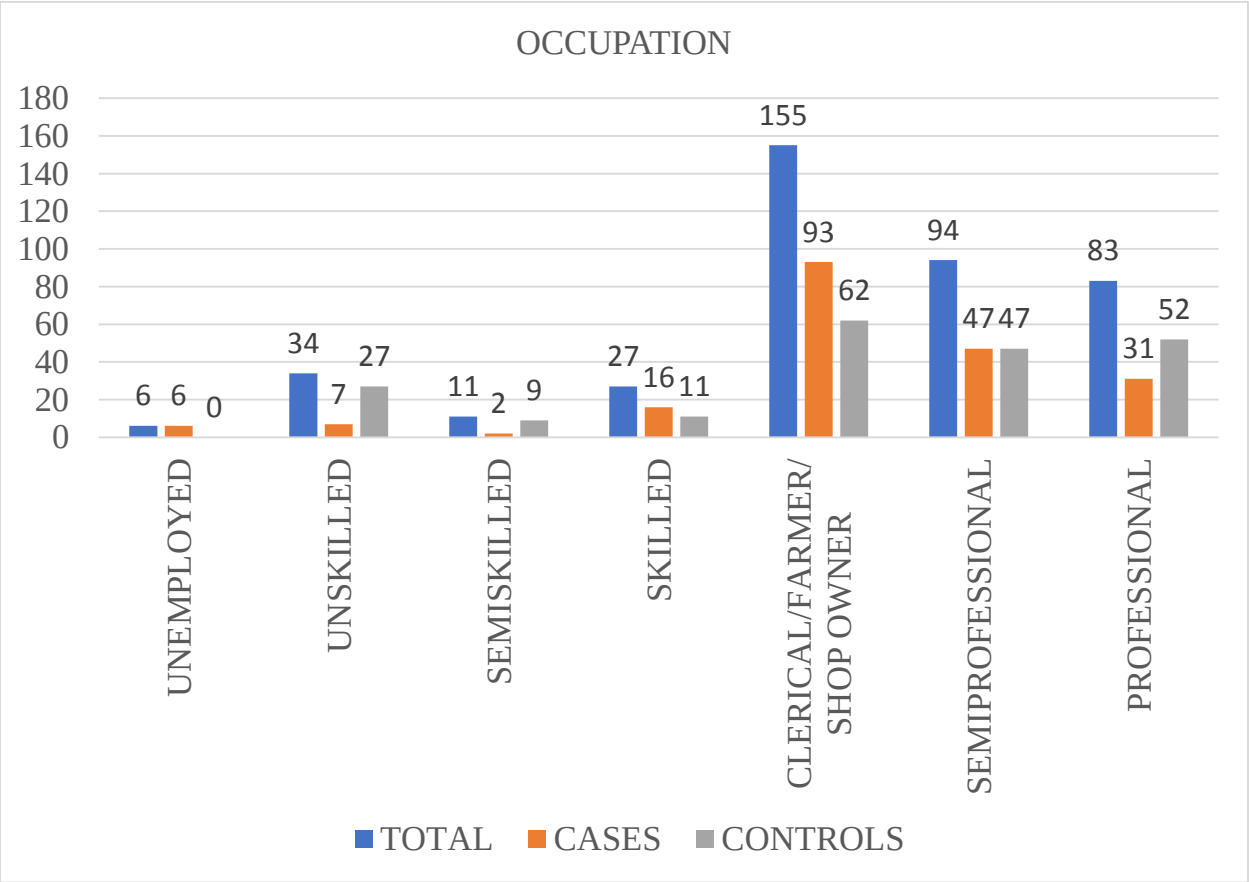


Figure 8: Occupation

MONTHLY INCOME

The distribution of income has been shown in the graph below.

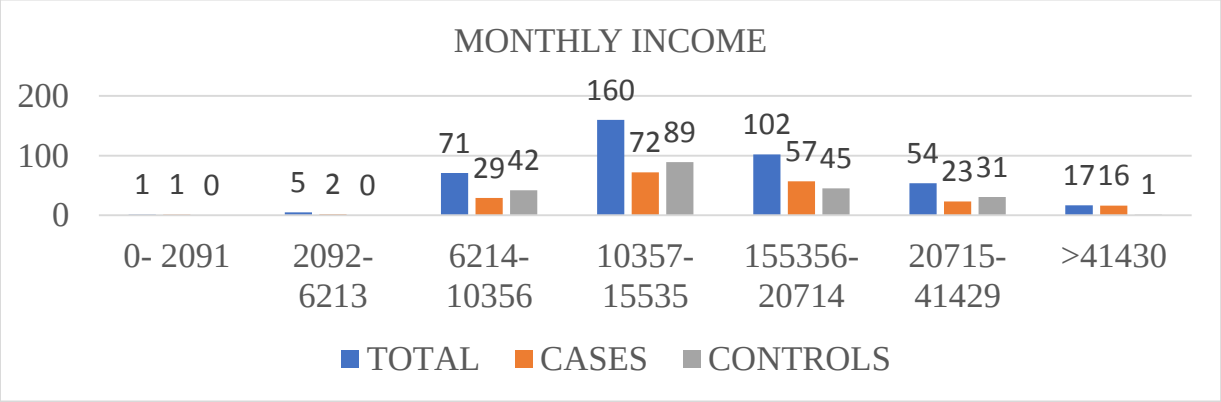


Figure 9: Monthly income

MODIFIED KUPPUSWAMY SES SCORE

The pie chart below demonstrates the modified kuppuswamy SES score. 42.4% belonged to the lower middle category. 13.4 % belonged to the upper lower category. 11.2% belonged to the upper category and 2.9% belonged to the upper middle category.

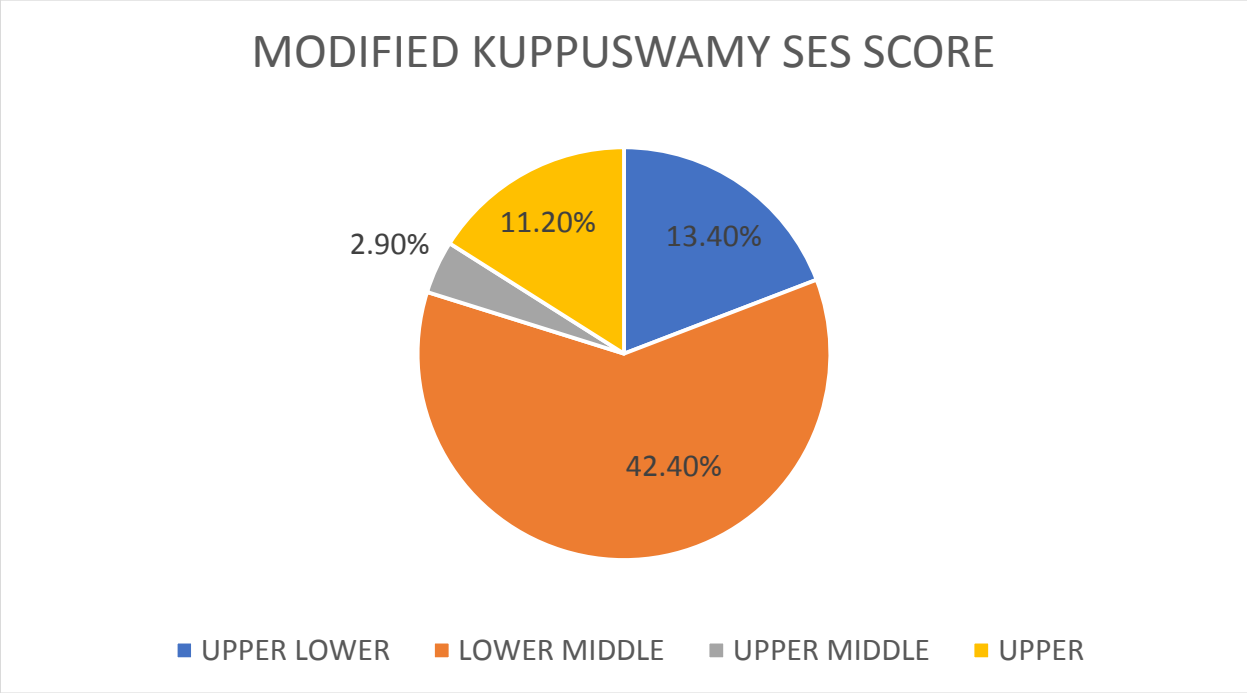


Figure 10: MODIFIED KUPPUSWAMY SES SCORE

RISK FACTORS ASSOCIATED WITH URINARY TRACT INFECTION

Elderly gravida versus urinary tract infection

Elderly gravida is defined as pregnancy at 35 years of age or above. Age more than or equal to 35 years is associated with adverse outcomes (43). . When we looked at the same with respect to risk of urinary tract infection in elderly women. There was no statistically significant difference between the two groups.

Table 7: Elderly gravida versus urinary tract infection.

ELDERLY GRAVIDA	Cases	Controls	OR	95 % CI	P value
Age≥ 35 years	5 (2.5%)	9 (4.3%)	0.561	0.185- 1.704	0.224
Age < 35 years	197 (97.5%)	199 (95.7%)			

Teenage pregnancy versus urinary tract infection

Similarly, teenage pregnancy which is defined as pregnancy at age of 19 years or less than 19 years is associated with adverse maternal and fetal outcomes (44). When we looked at the same with respect to risk of urinary tract infection. There was no statistically significant difference between the two groups.

Table 8: Teenage pregnancy versus urinary tract infection

TEENAGE PREGNANCY	Cases	Controls	OR	95% CI	P value
Age ≤ 19 y	3 (1.5%)	7 (3.4%)	0.433	0.110- 1.698	0.181
Age > 19 y	199 (98.5%)	201 (96.6%)			

Primigravida versus multigravida and risk of urinary tract infection

This table shows that primigravida patients had increased risk of urinary tract infection with OR of 1.458 and P value which was statistically significant.

Table 9: Parity versus urinary tract infection

PARITY	Cases	CONTROLS	OR	95% CI	P VALUE
PRIMIGRAVIDA	117 (57.92%)	101 (48.6%)	1.458	0.987 – 2.153	0.036
MULTIGRAVIDA	85 (42.1%)	107 (51.4%)			

Singleton versus Multifetal gestation versus UTI

Multifetal pregnancy can be associated with more adverse maternal and fetal outcomes and increased risk of urinary tract infection. The table below showed the increased risk of urinary tract infection in multifetal pregnancy with odds ratio of 8.53 (95% CI 1.05-68.8) which was statistically significant ($p<0.05$) (45).

Table 10: Multifetal pregnancy versus urinary tract infection.

	Cases	Controls	OR	95% CI	P value
Multifetal	8 (4%)	1 (0.5%)	8.53	1.05 to 68.88	0.044
Singleton	194 (96%)	207 (99l5%)			

Trimester at which UTI occurred

This study showed that urinary tract infection occurred most commonly in the third trimester followed by second trimester.

Table 11: Incidence of urinary tract infection in each trimester

TRIMESTER	FREQUENCY	PERCENTAGE
FIRST TRIMESTER	22	10.9 %
SECOND TRIMESTER	49	24.3 %
THIRD TRIMESTER	131	64.9 %

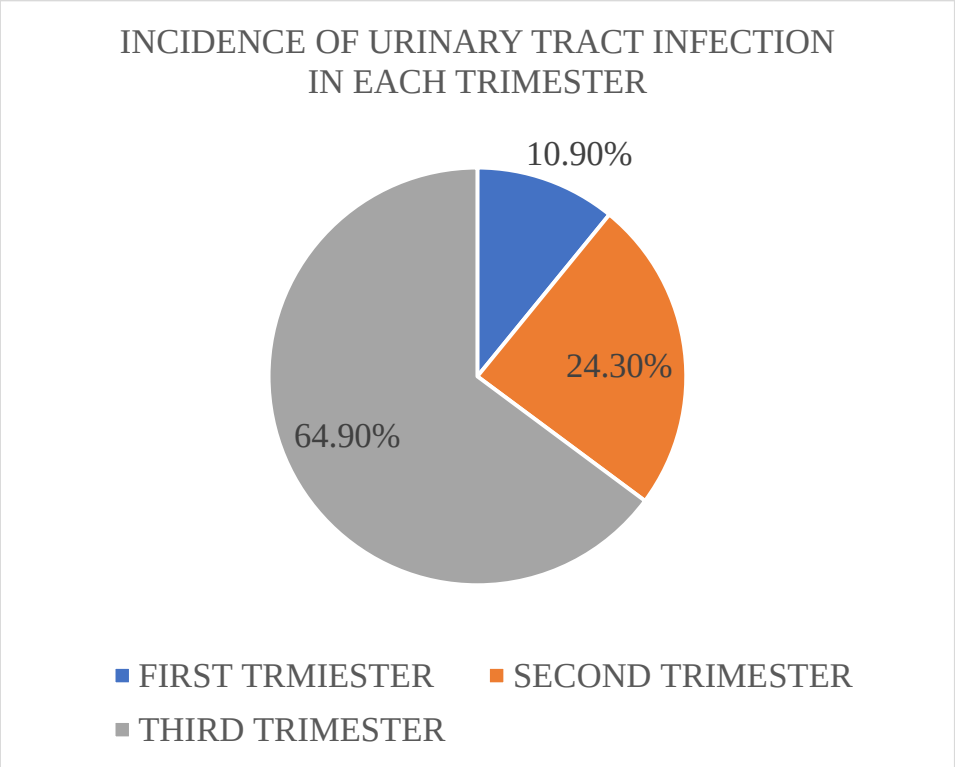


Figure 11: Incidence of urinary tract infection in each trimester

Fertility treatment versus UTI

In this study, 5% of the participants conceived following fertility treatment. The risk of urinary tract infection following assisted reproduction was looked at. There was no statistically significant risk of urinary tract infection following conception after fertility treatment.

Table 12: Fertility treatment and risk of urinary tract infection

FERTILITY TREATMENT	CASES (N)	CONTROL (N)	OR	95% CI	P VALUE
YES	13 (6.4%)	9 (4.32%)	1.521	0.635 - 3.641	0.897
NO	189 (93.6%)	199 (95.7%)			
TOTAL	202	208			

Abortion versus case and control

We looked at abortion as well as recurrent abortion as risk factor for urinary tract infection. There was no statistically significant association between abortion and risk of urinary tract infection.

Table 13: Abortion and urinary tract infection

ABORTION	CASES	CONTROLS	OR	95% CI	P VALUE
YES	41 (20.3%)	38 (18.3%)	1.139	0.697– 1.862	0.346
NO	161 (79.7%)	170 (81.7%)			

Table 14: Recurrent abortion and urinary tract infection.

RECURRENT ABORTION	CASES	CONTROLS	OR	95% CI	P VALUE
YES	15 (36.6%)	9 (23.7%)	1.859	0.697-4.960	0.158
NO	26 (63.4%)	29 (76.3%)			

Education versus case and control

The impact of education on risk of urinary tract infection was looked at. Participants were divided into 2 groups. Low education group comprised of participants who have education up to middle school certificate. High education group refers to participants who have completed high school certificate or beyond. Low level of maternal education is associated with adverse maternal and fetal outcomes and increased risk of urinary tract infection as shown by OR of 1.83 (95%CI 1.03 – 3.24, $p<0.05$)

Table 15: Maternal education and urinary tract infection

EDUCATION	CASES	CONTROLS	OR	95% CI	P VALUE
Low education	36 (17.8%)	22 (10.6%)	1.834	1.03 – 3.24	0.025
High education	166 (82.2%)	186 (89.4%)			

Kuppuswamy SES versus urinary tract infection.

Participants were categorized as low SES which included participants falling into upper lower, lower middle and upper middle. High SES included participants who belonged to upper SES status as per Kuppuswamy score. There was no statistically significant association between SES score and risk of urinary tract infection.

Table 16: Kuppuswamy SES score and urinary tract infection

SES	CASES	CONTROL	OR	95% CI	P VALUE
LOW SES	182 (90.1%)	182 (87.5%)	0.404	0.70- 2.41	0.173
HIGH SES	20 (9.9%)	26 (12.5%)			

Genitourinary abnormality versus case and control

There were a total of 15 patients with genitourinary abnormality. These various genitourinary abnormalities seen are summarized in the table below. The most common was renal calculi with hydroureteronephrosis, followed by fibroid uterus, bicornuate uterus, unicornuate uterus and vaginal stenosis. 9 of these had urinary tract infections and 6 did not have urinary tract infection. There was no statistically significant association between genitourinary abnormality and risk of urinary tract infection.

Table 17: Genitourinary abnormalities

Genitourinary abnormality	Number
Renal calculi with Hydroureteronephrosis	4
Fibroid uterus	3
Bicornuate uterus	2
Unicornuate uterus	2
Septate uterus	1
Vaginal septum	1
Vaginal stenosis	2
Total	15

Table 18: Genitourinary abnormality and urinary tract infection.

Genitourinary abnormality	Cases	Control	OR	95% CI	P value
Yes	9 (4.5%)	6 (2.9%)	1.753	0.625-4.918	0.205
No	193 (95.5%)	202 (97.1%)			

Past history of catheterization

A total of 34 patients had past history of urinary tract infection. Of these, 24 were cases and 10 were controls. Past history of catheterization were associated with increased risk of urinary tract infection with an odds ratio of 2.670 (95% CI 1.24- 5.737, p= 0.007).

Table 19: Past history of catheterization and urinary tract infection

Past history of catheterization	CASES	CONTROLS	OR	95% CI	P VALUE
YES	24 (11.9%)	10 (4.8%)	2.670	1.24-5.737	0.007
NO	178 (88.1%)	198 (95.2%)			

Past history of UTI

There were 4 patients with past history of urinary tract infection. All four patients developed symptomatic urinary tract infection during the antenatal period. This was statistically significant (p= 0.058)

Table 20: Past history of UTI

PAST HISTORY OF UTI	CASES	CONTROL	P VALUE
YES	4	0	0.058
NO	198	208	

Gestational diabetes mellitus and urinary tract infection

There were 49 patients with GDM in the cases and 53 patients in the controls. There was no statistically significant risk of urinary tract infection in pregnant women with GDM.

Table 21: GDM and UTI

GESTATIONAL DM	CASES	CONTROLS	OR	95% CI	P VALUE
YES	49 (24.3%)	53 (25.5%)	0.937	0.598 – 1.466	0.432
NO	153 (75.7%)	155 (74.5%)			

Pregestational diabetes mellitus and urinary tract infection

The number of participants with pregestational diabetes mellitus was 6 which was 1.5% of the participants studied. There was no statistically significant increase in urinary tract infection among pregnant women with pregestational DM.

Table 22: Pregestational DM and UTI

PREGESTATIONAL DM	CASES	CONTROLS	OR	95% CI	P VALUE
PRESENT	5 (2.5%)	1 (0.5%)	5.254	0.608-45.369	0.101
ABSENT	197 (97.5%)	207 (99.5%)			

Chronic hypertension and urinary tract infections

The incidence of chronic hypertension between cases and control were looked at. There were only 3 cases and 5 controls with chronic hypertension. There was no statistically significant increase in urinary tract infection risk among cases and controls with chronic hypertension.

Table 23: Chronic hypertension and UTI

HTN	CASES	CONTROL	OR	95% CI	P VALUE
HTN YES	3 (1.5%)	5 (2.4%)	0.612	0.144- 2.595	0.378
HTN NO	199 (98.5%)	203 (97.6%)			

Anemia as a risk factor for UTI.

Anemia during pregnancy is associated with adverse outcomes. Anemia during pregnancy is classified by ICMR as mild, moderate and severe. Mild anemia is 10 to 11 g/dl. Moderate anemia is 7 to 10g/dl and severe anemia is 4 to 7 mg/dl (46). This study done showed that anemia is associated with urinary tract infection with Odds ratio of 1.48 which was statistically significant (p= 0.05).

Table 24: Anemia and UTI

Hb < 11g/dl	CASES	CONTROLS	OR	95% CI	P VALUE
YES	65 (32.5%)	51 (24.6%)	1.484	0.973 – 2.263	0.05
NO	135 (67.5%)	156 (75.4%)			

SUMMARY OF RISK FACTORS ASSOCIATED WITH URINARY TRACT INFECTION

Risk factor	Cases N= 202	Controls N= 208	Or	95% ci	P value
Elderly gravida (Age >/= 35 yrs)	5 (2.5%)	9 (4.3%)	0.561	0.185- 1.704	0.224
Teenage pregnancy (Age </= 19 yrs)	3 (1.5%)	7 (3.4%)	0.433	0.110- 1.698	0.181

Primigravida	117 (57.92%)	101 (48.6%)	**1.458**	**0.987 – 2.153**	**0.036**
Multifetal pregnancy	8 (4%)	1 (0.5%)	**8.53**	**1.05 to 68.88**	**0.044**
Fertility treatment	13 (6.4%)	9 (4.3%)	1.521	0.635 - 3.641	0.897
Abortion	41 (20.3%)	38 (18.3%)	1.139	0.697– 1.862	0.346
Recurrent abortions	15 (36.6%)	9 (23.7%)	1.859	0.697- 4.960	0.158
Low Maternal education	36 (17.8%)	22 (10.6%)	**1.834**	**1.037 – 3.243**	**0.025**
Low Kuppuswamy SES scale	182 (90.1%)	182 (87.5%)	0.404	0.70- 2.41	0.173
Genitourinary abnormality	9 (4.5%)	6 (2.9%)	1.753	0.625- 4.918	0.205
Past history of Catheterization	24 (11.9%)	10 (4.8%)	**2.670**	**1.24- 5.737**	**0.007**
Gestational DM	49 (24.3%)	53 (25.5%)	0.937	0.598 – 1.466	0.432
Pregestational DM	5 (2.5%)	1 (0.5%)	5.254	0.608- 45.369	0.101
Chronic hypertension	3 (1.5%)	5 (2.4%)	0.612	0.144- 2.595	0.378
Anemia Hb < 11g/dl	65 (32.5%)	51 (24.6%)	**1.484**	**0.973 – 2.263**	**0.05**

MATERNAL OUTCOMES

Urinary tract infection can be associated with adverse maternal outcomes such as premature delivery, low birth weight infants, placental abruption, pre-eclampsia, premature rupture of membranes, preterm premature rupture of membranes, chorioamnionitis, and renal complications like pyelonephritis, LSCS (41).

Placental abruption

Out of the 410, patients studied, placental abruption occurred in 2.5% of pregnant women with UTI and 1.9 % of women without UTI. The odds ratio was 1.29 (95% CI: 0.343-4.891). The difference was not statistically significant (p=0.482).

Gestational Hypertension and mild pre-eclampsia

Out of the 410 patient's studied, Gestational hypertension and mild pre –eclampsia occurred in 6.4% women with UTI versus 4.3% women without UTI. The odds ratio was 1.521 (95% CI: 0.635- 3.641). The difference was not statistically significant (p=0.234).

Severe preeclampsia to eclampsia

Out of the 410 patients studied, severe pre-eclampsia to eclampsia occurred in 5.4% women with UTI versus 4.8% women without UTI. The odds ratio was 1.076 (95% CI: 0.473-2.747). The difference was not statistically significant (p=0.472).

Premature rupture of membranes

Out of the 410 patients studied, premature rupture of membranes occurred in 2.0% women with UTI versus 3.8 % women without UTI. The odds ratio was 0.505 (95% CI: 0.150-1.704). The difference was not statistically significant (p=0.205).

Preterm premature rupture of membranes

Out of the 410 patients studied, preterm premature rupture of membranes occurred in 17.3 % women with UTI versus 7.2 % women without UTI. The odds ratio was 2.697 (95% CI: 1.423- 5.111). The difference was statistically significant (p=0.001).

Table 25: PPROM and UTI

PPROM	CASES (N)	CONTROLS (N)	OR	95% CI	P VALUE
YES	35 (17.3%)	15 (7.2%)	2.697	1.423 – 5.111	0.001
NO	167 (82.7%)	193 (92.8%)			

Preterm delivery.

Out of the 410 patients studied, preterm labor occurred in 28.2 % women with UTI versus 11.1 % women without UTI. The odds ratio was 3.162 (95% CI: 1.860 – 5.376). The difference was statistically significant ($p<0.05$).

Table 26: Preterm delivery versus UTI

PRETERM	CASES	CONTROLS	OR	95% CI	P VALUE
YES	57 (28.2%)	23 (11.1)	3.162	1.860 – 5.376	<0.05
NO	145 (71.8%)	185 (88.9%)			

Chorioamnionitis

There were four cases of chorioamnionitis which occurred among the cases. There were no cases of chorioamnionitis among the controls. This showed that urinary tract infection during pregnancy predisposed the patient to chorioamnionitis which was statistically significant. ($p< 0.05$)

Pyelonephritis

There were 17 cases of pyelonephritis among the cases. There were no cases of pyelonephritis among the controls. Of these 17 cases, 8 had positive growth on blood culture, 4 patients had renal angle tenderness, and 5 patients fulfilled criteria for systemic inflammatory response syndrome. This showed that there was increased incidence of pyelonephritis among the cases as compared to the controls which was statistically significant ($p<0.05$).

Postpartum sepsis

Out of the 410 patients studied, postpartum sepsis occurred in 8.9 % women with UTI versus 2.4 % women without UTI. The odds ratio was 3.972 (95% CI: 1.446 – 10.912). The difference was statistically significant (p=0.003).

Table 27: Postpartum sepsis and UTI

POSTPARTUM SEPSIS	CASES	CONTROLS	OR	95% CI	P VALUE
YES	18 (8.9%)	5 (2.4%)	3.972	1.446 – 10.912	0.003
NO	184 (91.1%)	203 (97.6%)			

Intrauterine growth restriction (IUGR)

Out of the 391 patients studied, IUGR occurred in 18.3 % women with UTI versus 11.7 % women without UTI. The odds ratio was 1.687 (95% CI: 0.959 – 2.969). The difference was statistically significant (p=0.046).

Table 28: IUGR and UTI

IUGR	CASES	CONTROLS	OR	95 % CI	P VALUE
YES	34 (18.3%)	24 (11.7%)	1.687	0.959 – 2.969	0.046
NO	152 (81.7%)	181 (88.3%)			

Normal versus Instrumental and Caesarean delivery

Out of the 410 patients studied, instrumental and caesarean delivery occurred in 50 % women with UTI versus 44.7 % women without UTI. The odds ratio was 1.237 (95% CI: 0.839 – 1.823). The difference was not statistically significant (p=0.165).

SUMMARY OF MATERNAL OUTCOMES

Table 29: SUMMARY OF MATERNAL OUTCOMES

	CASES	CONTROLS	OR	95% CI	P VALUE
Placental abruption	5 (2.5%)	4 (1.9%)	1.294	0.343- 4.891	0.482
Gestational hypertension to mild pre-eclampsia	13 (6.4%)	9 (4.3%)	1.521	0.635- 3.641	0.234
Severe pre eclampsia to eclampsia	11 (5.4%)	10 (4.8%)	1.140	0.473- 2.747	0.472
Premature rupture of membranes	4 (2%)	8 (3.8%)	0.505	0.150- 1.704	0.205
Preterm premature rupture of membranes	35 (17.3%)	15 (7.2%)	**2.697**	**1.423- 5.111**	**0.001**
Preterm delivery	57 (28.2%)	23 (11.1%)	**3.162**	**1.860- 5.376**	**0.000**
Postpartum sepsis	18 (8.9%)	5 (2.4%)	**3.972**	**1.46- 10.91**	**0.003**

Intrauterine growth restriction	34 (18.3%)	24 (11.7%)	**1.697**	**0.959- 2.969**	**0.046**
Instrumental and caesarean deliveries	101 (50%)	93 (44.7%)	1.237	0.839- 1.823	0.165

FETAL OUTCOMES

LOW BIRTHWEIGHT

Out of 390 patient studied, low birth weight occurred in 30.6 % of pregnant women with UTI versus 16.2% women without UTI. The odds ratio was 2.290 (95% CI: 1.409 – 3.722). The difference was statistically significant (p=0.001).

Table 30: Low birth weight and UTI

LOW BIRTH WEIGHT	CASES	CONTROLS	OR	95% CI	P VALUE
YES	57 (30.6%)	33 (16.2%)	2.290	1.409 – 3.722	0.001
NO	129 (69.4%)	171 (83.8%)			

NEONATAL ICU ADMISSION

Out of 391 patient studied, neonatal ICU admission occurred in 76.2 % of pregnant women with UTI versus 42.1% women without UTI. The odds ratio was 4.406 (95% CI: 2.370 – 8.189). The difference was statistically significant (p <0.05).

Table 31: Neonatal ICU admission

	NICU YES	NICU NO	OR	95 % CI	P VALUE
CASES	48 (76.2%)	138 (42.1)	4.406	2.370 – 8.189	<0.05
CONTROLS	15 (23.8%)	190 (57.9%)			

APGAR < 7 AT 1 MIN

Out of 391 patient studied, low APGAR occurred in 3.8 % of pregnant women with UTI versus 3.4% women without UTI. The odds ratio was 1.106 (95% CI: 0.381 – 3.215). The difference was not statistically significant (p=0.533).

APGAR < 7 AT 5 MIN

Out of 391 patient studied, low APGAR occurred in 1.6 % of pregnant women with UTI versus 0.5 % women without UTI. The odds ratio was 3.344 (95% CI: 0.345 – 32.434). The difference was not statistically significant (p=0.276).

SUMMARY OF FETAL OUTCOMES

Table 32: Summary of fetal outcomes

	CASES	CONTROLS	OR	95 % CI	P VALUE
LOW BIRTH WEIGHT	57 (30.6%)	33 (16.2%)	**2.290**	**1.409- 3.722**	**0.001**
NICU ADMISSION	48 (25.8%)	15 (7.3%)	**4.406**	**2.370- 8.189**	**<0.05**
APGAR <7 AT 1 MIN	7 (3.8%)	7 (3.4%)	1.106	0.381- 3.215	0.533
APGAR < 7 AT 5 MIN	3 (1.6%)	1 (0.5%)	3.344	0.345- 32.434	0.276

MULTIVARIATE ANALYSIS

On multivariate analysis, the following factors were statistically significant after adjusting for confounding factors. This showed that low maternal education and past history of catheterization increases the risk of symptomatic urinary tract infection during pregnancy which in turn predisposes to preterm delivery and post-partum sepsis.

Table 33: Multivariate analysis

	OR	95% CI	P VALUE
Preterm delivery	3.066	1.797- 5.233	P <0.05
Low maternal education	1.980	1.096- 3.574	P= 0.023
Post-partum sepsis	3.585	1.264- 10.171	P= 0.016
Past history of Catheterization	2.684	1.220- 5.905	P= 0.014

ORGANISMS CAUSING URINARY TRACT INFECTION

This study showed a total of 214 episodes of urinary tract infection. 11 participants in the cases arm had 2 episodes of urinary tract infection and 1 patient had 3 episodes of urinary tract infection during their antenatal period.

Table 34: Recurrent urinary tract infection

NUMBER OF URINARY TRACT INFECTION	NUMBER OF CASES
1 EPISODE OF URINARY TRACT INFECTION	202

2 EPISODES OF URINARY TRACT INFECTION	11
3 EPISODES OR URINARY TRACT INFECTION	1
TOTAL	214

The most common organism causing urinary tract infection was E. coli followed by Klebsiella. Other organisms causing urinary tract infection were Citrobacter species, non fermenting gram negative bacilli, Enterobacter, Serratia, Aeromonas, Enterococcus, Streptococci, Staphylococcus species and Pseudomonas.

Table 35: Organisms causing UTI

ORGANISMS	NUMBER	PERCENTAGE
E.COLI	115	53.7%
KLEBSIELLA	43	20.1%
ENTEROCOCCUS	45	21.02%
STREPTOCCUS	14	6.5%
CITROBACTER	9	4.2%

STAPHYLOCOCCUS	9	4.2%
NFGNB	10	4.7%
PSEUDOMONAS	5	2.3%
ENTEROBACTER	4	1.9%
SERRATIA	2	0.93%
AEROMONAS	1	0.47%

We also looked at the antimicrobial susceptibility pattern of the organisms causing urinary tract infection. 40.8% of the E.coli were extended spectrum beta lactamase producers. 23.3% of Klebsiella were ESBL producers.

There was only 1 patient with Enterococcus which was resistant to Ampicillin.

Staphylococcus species were found to cause 4.2% of urinary tract infection. The species cultures included Staphylococcus aureus and Staphylococcus saprophyticus.

There were 5 patients who grew Pseudomonas species in the urinary culture. All of them were susceptible to Piperacillin Tazobactum, Levofloxacin and Cefoperazone sulbactum.

DISCUSSION

Urinary tract infection during pregnancy is associated with adverse maternal and fetal outcomes as shown by various studies done. This is potentially a preventable cause for adverse maternal and fetal outcomes by early detection and appropriate treatment of infection. Most of the studies on urinary tract infection have come from the western literature. Therefore, it is necessary to know the prevalence of the same in India and ensure early detection and treatment of urinary tract infection.

This is a cross sectional study which has recruited 410 pregnant women between July 2017 and August 2018. 9 were multifetal pregnancies. The incidence of pyelonephritis was 8% in our institution which was higher than that published in western literature of 0.5 to 2% (6). The increase in incidence of pyelonephritis is due to severe reasons such as increased prevalence of symptomatic urinary tract infection in India as compared to Western population and referral bias in view of this institution being a tertiary care center.

This study also looked at risk factors which predisposed to urinary tract infection. Elderly gravida is associated with adverse outcomes (43). In this study there was no statistically significant increased risk of UTI in elderly gravida. This could be because there were only 14 pregnant women who were 35 years of age or older. We also looked at whether teenage pregnancy increased the risk of urinary tract infection. Teenage pregnancy is associated with numerous adverse outcomes such as preterm delivery, low birth weight and neonatal mortality as shown by Chen et al(44). There were no studies which looked at the prevalence of UTI in teenage pregnancy. Our study had 10 patients with teenage pregnancy

of which 3 developed symptomatic urinary tract infection. This was not statistically significant however.

Our study also looked at parity and risk of urinary tract infection. Emiru et al had shown that parity was not statistically associated with risk of urinary tract infection(10). Our study showed that primigravida had increased risk of urinary tract infection which was statistically significant with OR of 1.458 (95% CI 0.987- 2.153, p=0.036). Study done by Wing et al in 2014, showed that multiparous women had reduced incidence of urinary tract infection as compared to nulliparous women (6). This could be attributed to the better awareness of pregnancy complications in multiparous women as compared to nulliparous women (47).

Multifetal pregnancy was associated with increased risk of urinary tract infection which was consistent with the findings of Dotters-Ketz et al in 2015 which had shown that multifetal pregnancy had increased risk of urinary tract infection with OR of 3.01 (95 % CI 2.93 to 3.09) (45). Our study showed similar findings with OR of 8.53 (95% CI of 1.05 to 68.8, p= 0.04). This could be explained by the higher progesterone levels in multifetal pregnancy, increase in size of the renal collecting system when compared to singleton pregnancy and by gravid uterus causing compression of the ureters which increases the risk for urinary tract infection (45).

When we looked at the incidence of urinary tract infection as per each trimester, it was seen that UTI occurred most commonly in the third trimester. This can be explained by the gravid uterus causing obstruction to the genitourinary system and hence predisposing to UTI.

Study done by Mazor-Dray et al in 2009 looked at 199,093 deliveries. This study showed that pregnant women who developed UTI had statistically significant higher number of patients who underwent fertility treatment as compared to pregnant women who did not develop UTI (41). Our study had 22 patients who conceived following fertility treatment. However, there was no statistical significant association between fertility treatment and UTI. This could be because of the lower number of pregnant women who were studied in this study. There was no association between abortion and risk of urinary tract infection.

Low maternal education is associated with adverse pregnancy outcomes as shown by study done by Muttai et al in Kenya (48). However, it did not look at urinary tract infection and association with maternal education. Emiru et al looked at education as a risk factor of UTI and found that there was no statistically significant association between the same. Wing et al showed that lower maternal education, which was defined as less than 12 years of formal education, was associated with increased risk of UTI with OR of 1.5 (95% CI 1.4- 1.7) (6). Our study done showed that low maternal education, which was defined as less than completion of high school was associated with increased risk of urinary tract infection with OR of 1.834 (95% CI 1.03- 3.24, $p < 0.05$). There was no association between low kuppuswamy SES score and adverse maternal outcomes.

Gestational DM is associated with increased risk of urinary tract infection as shown by McMahon et al (11). Our study did not show any statistically significant association. This could be because of the early detection of GDM through universal screening, aggressive management of uncontrolled diabetes through obstetric medicine clinics and gestational DM clinics and careful follow up of patients.

Pregestational DM and chronic hypertension did not have statistically significant association with risk of urinary tract infection.

Anemia during pregnancy is associated with adverse outcomes. Anemia increases the risk of urinary tract infection has been shown by Schieve et al in 1994 (49). Our study showed that hemoglobin less than 11 g/dl is associated with increased risk for urinary tract infection with OR of 1.484 (95% CI 0.973- 2.263, $p<0.05$).

This study then looked at maternal outcomes secondary to urinary tract infection. There was increased incidence of preterm premature rupture of membranes among pregnant women with urinary tract infection as compared to pregnant women without urinary tract infection in our study and this was statistically significant with OR of 2.697 (95% CI 1.423-5.11, p= 0.001). Urinary tract infection predisposes to PPROM has been seen in various studies. Mazor-Dray et al in 2009 showed increased risk of PPROM in pregnant women with UTI with OR 1.5 (95% CI 1.4- 1.7) and increased incidence of preterm delivery with OR 2.1 (95% CI 1.9-2.3, $p<0.05$) (41). There was increased incidence of preterm delivery in our study which was also statistically significant with OR of 3.162 (95% CI 1.860-5.376, $p<0.05$). Pregnant women with urinary tract infection also had increased incidence of post-partum sepsis (OR 3.972, 95% CI 1.446- 10.912, p= 0.003) and intrauterine growth restriction (OR 1.697, 95% CI 0.959- 2.969, p=0.046) which were all statistically significant and similar to study findings of Mazor-Dray et al (41). There was no statistically significant difference in the number of normal versus LSCS or Instrumental delivery in association with urinary tract infection. This could be because of early detection of UTI

and appropriate treatment for the same, lesser number of LSCS that happen in our hospital as compared to Western population.

When we looked at fetal outcomes, low birth weight and neonatal ICU admission were increased among pregnant women with urinary tract infection as compared to pregnant women without UTI which were statistically significant with low birth weight having OR of 2.29 (95% CI 1.409- 3.722, p= 0.001) and neonatal ICU admission having OR of 4.406 (95% CI 2.370- 8.189, p <0.05). Increased incidence of low birth weight among pregnant women with UTI was shown in numerous studies such as that done by Wing et al, Mazor-Dray et al, and Schieve et al (6,41,49). UTI predisposed to preterm labor which leads to low birth weight and increased neonatal ICU admission for preterm care.

When multivariate analysis was done, low maternal education and past history of catheterization predisposing to symptomatic urinary tract infection were statistically significant (OR 1.989, 95% CI 1.096- 3.574, p= 0.023 ; OR 2.684, 95% CI 1.220- 5.905, p=0.014) . Preterm delivery and post-partum sepsis were statistically significant in multivariate analysis (OR 3.066, 95% CI 1.797- 5.233, p< 0.05; OR 3.585, 95% CI 1.264-10.171, p=0.016).

We then looked at the organisms causing urinary tract infection. Most common organism causing UTI was E.coli followed by Klebsiella. The antimicrobial susceptibility data showed that 40.8% of the E.coli were extended spectrum beta lactamase producing E.coli and 23.3% of the Klebsiella were extended spectrum beta lactamase producing Klebsiella. There was no significant difference in outcome of urinary tract infection caused by ESBL producing organism versus non ESBL producing organism

LIMITATIONS

There were a few limitations in this study. Firstly, we did not achieve the sample size which we intended to, due to slow recruitment. However, to the best of our knowledge this would be one of the first studies in CMC, which looked at risk factors, maternal outcomes, and fetal outcomes, organisms causing urinary tract infection and antimicrobial susceptibility pattern for the same. Therefore, this study, despite its small sample size, provides a scaffolding for further research, especially in identifying risk factors, predictors and treatment options.

Secondly, in view of being a tertiary care center, there is referral bias which tends to overestimate the adverse maternal and fetal outcomes.

Thirdly, as we recruited pregnant women after delivery, administrating the questionnaire was cumbersome and could have resulted in false reporting by the patient.

Fourthly, the symptoms seen in urinary tract infection can also be seen in pregnancy and during labour which makes it difficult to assess if they are having symptomatic urinary tract infection.

Fifthly, the assessment of family income, and socioeconomic status may not have been accurate as patient and family tend to underplay their profession and income so as to attain financial support from the institution.

CONCLUSIONS

In conclusion, this cross sectional study done on pregnant women showed that urinary tract infection during pregnancy is associated with adverse maternal and fetal outcomes. This can ideally be prevented by screening for asymptomatic bacteriuria and early appropriate antibiotic therapy to prevent symptomatic urinary tract infection. Patient with risk factors for urinary tract infection need to be identified early and precautions need to be taken to prevent development of the same.

Future research must be aimed at ensuring larger number of patient recruitment with emphasis on good follow-up by using the same model as we used in this study. We should also look at the incidence of asymptomatic bacteriuria and the adverse maternal and fetal outcomes associated with same, as the group has more adverse outcomes as they do not seek therapy, given they are asymptomatic.

In addition, studies must be done to elucidate the pathogenesis for urinary tract infection, even though there are proposed theories, but none have been conclusively proven. We must perform studies to look at the cytokine and interleukin levels at baseline, end of each trimester and following a urinary tract infection.

In conclusion, early detection and treatment for symptomatic urinary tract infection prevents adverse maternal and fetal outcomes and reducing mortality and morbidity. This is a preventable cause of mortality. Various actions at the national health policy level need to be implemented to prevent the same

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ANNEXURES

DATA ENTRY FORM

PROTOCOL ID ☐☐☐☐

DEPARTMENT ☐☐☐☐ AGE IN YEARS ☐☐ OBSTETRIC SCORE ☐☐☐☐

PARITY- ☐ PRIMIGRAVIDA $_1$ MULTIGRAVIDA $_2$ GRAND MULTIGRAVIDA$_3$

☐ SINGLETON$_1$ MULTIFETAL PREGNANCY $_2$

RISK FACTORS

FERTILITY TREATMENT-☐ YES $_1$ / NO $_2$

IF YES- ☐ OVULATION INDUCTION$_1$/ICSI$_2$/IVF$_3$/GIFT$_4$/ZIFT$_5$/OTHERS$_6$/MORE THAN ONE$_7$

IF OTHERS, MENTION ☐☐☐☐☐☐☐☐☐

NUMBER OFABORTIONS ☐ **NUMBER OF CONSECUTIVE ABORTIONS** ☐

EDUCATIONAL STATUS ☐ ILLITERATE$_1$/ PRIMARY SCHOOL CERTIFICATE$_2$/ MIDDLE SCHOOL CERTIFICATE$_3$/ HIGH SCHOOL CERTIFICATE$_4$/ INTERMEDIATE OR POST HIGH SCHOOL DIPLOMA$_5$/ GRADUATE OR POST GRADUATE$_6$/ PROFESSIONAL OR HONOURS$_7$.

OCCUPATION ☐ PROFESSION$_{10}$/ SEMI PROFESSION$_6$/ CLERICAL, SHOP OWNER, FARMER$_5$/ SKILLED$_4$/ SEMISKILLED$_3$/ UNSKILLED$_2$/ UNEMPLOYED$_1$.

FAMILY MONTHLY INCOME ☐ >/= 42,876$_{12}$/ 21,438- 42,875$_{10}$/ 16,078- 21,437$_6$/ 10,719- 16,077$_4$/ 6,431- 10,718$_3$/ 2,165- 6,430$_2$/ </= 2,164$_1$

MODIFIED KUPPUSWAMY SES SCALE ☐< 5= LOWER$_1$/ 5-10= UPPER LOWER$_2$/ 11-15= LOWER MIDDLE$_3$/ 16- 25= UPPER MIDDLE$_4$/ 26-29 = UPPER$_5$

TRIMESTER AT WHICH UTI OCCURRED TRIMESTER$_1$/ SECOND TRIMESTER$_2$/ THIRD TRIMESTER

GENITOURINARY ABNORMALITY ☐ YES$_1$ / NO$_2$

PAST HISTORY OF CATHETERIZATION IN THE LAST 10 YEAR ☐ YES$_1$ / NO$_2$

NUMBER OF TIMES CATHETERIZED ☐☐ INDICATION FOR CATHETERIZATION ☐

DURATION OF EACH CATHETERIZATION ☐☐

PAST HISTORY OF UTI IN LAST 10 YEARS ☐ YES$_1$ / NO$_2$

YEAR	ORGANISM ISOLATED	SUSCEPTIBILITY PATTERN

HEMOGLOBIN ☐☐ < 11$_1$ / <10 $_2$ / <7 $_3$

GESTATIONAL DIABETES MELLITUS ☐ YES/NO IF YES OHA_1/ $INSULIN_2$/$DIET_3$ ☐

PREGESTATIONAL DIABETES ☐ YES/NO IF YES OHA_1/ $INSULIN_2$/$DIET_3$ ☐

CHRONIC HYPERTENSION ☐ YES/NO

S NO	**ORGANISM ISOLATED**	**COLONY COUNTS**	**SUSCEPTIBILITY PATTERN**
1.	GNB		AUG AMI CEFPERSUL NITRO SEPTRAN GENTA CEFPOD CIPRO
2.	ENTEROCOCCUS		NITRO AMPI GENTA
3.	STREPTOCOCCI-B		PENICILLIN ERYTHROMYCIN
4.			

MATERNAL OUTCOMES

PLACENTAL ABRUPTION ☐ YES/NO

GESTATIONAL HYPERTENSION TO MILD PREECLAMPSIA ☐ YES/NO

SEVERE PRE ECLAMPSIA TO ECLAMPSIA ☐ YES/NO

PROM ☐ YES/NO PRETERM ☐ YES/ NO

PPROM ☐ YES/ NO POST PARTUM SEPSIS ☐ YES/ NO

CHORIOAMNIONITIS ☐ YES/NO

PYELONEPHRITIS ☐ POSITIVE BLOOD $CULTURE_1$/ RENAL ANGLE $TENDERNESS_2$/ $SONOLOGY_3$/ $SIRS_4$

NORMAL/ INSTRUMENTAL DELIVERY ☐ $NORMAL_1$/ LOW $FORCEPS_2$/ HIGH $FORCEPS_3$/ SUCTION CUP_4

CESAREAN DELIVERY ☐ YES/NO

ICU ADMISSION ☐ YES/NO

DURATION OF STAY IN ICU ☐☐ INOTROPES ☐ YES/NO MECHANICAL VENTILATION ☐ YES/NO

DURATION OF IN HOSPITAL STAY ☐☐

DEATH ☐ YES/NO IF YES, CAUSE OF DEATH

FETAL OUTCOMES

IUGR ☐ YES/NO

GESTATIONAL AGE AT BIRTH IN WEEKS ☐☐☐

BIRTH WEIGHT IN KG ☐☐

APGAR AT 1 MIN ☐ 5 MIN ☐

DEATH ☐ YES/NO LIVE BORN/ STILL BORN

NICU ADMISSION ☐ YES_1/ NO_2 IF YES, REASON

Christian Medical College, Vellore

Department of General Medicine III

PATIENT INFORMATION SHEET

Assessment of maternal outcomes and fetal outcomes secondary to urinary tract infection in pregnancy

Purpose of research:

You are being requested to participate in a study to see the adverse effects of urinary tract infection during pregnancy so as to see whether prevention of urinary tract infection during pregnancy can improve maternal and fetal outcomes. There is increased risk for urinary tract infection during pregnancy due to the body changes that occur during pregnancy. Early detection and appropriate treatment of the same may help to reduce the adverse maternal and fetal outcomes that can occur.

If you take part what will you have to do?

If you agree to participate in this study, you will be interviewed to see whether you have any risk factors that predispose to urinary tract infection and also to assess the increase in expenditure due to UTI. You will also be followed up till delivery to see the number of hospital visits required, number of UTIs, what treatment you received, and to assess adverse outcomes that have occurred to you as well as to the baby in case of the same. By giving consent, you are also giving permission to access your medical records for this study purpose.

What are the risks or benefits to you?

By participating in this study, you are not expected to have any risks or benefits. The study is purely observational, which means that participating in the study will not affect the course of your treatment. We are hoping that the results of this study will help us to reduce the adverse outcomes of urinary tract infection during pregnancy by early detection and appropriate treatment of the same.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you as it is a purely observational study.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask

Dr. Anjely Pulparampil Sebastian

Post Graduate Resident

Department of General Medicine Unit III

CMC Vellore.

Ph: 0416 2282039

Ph: 9751719991

Informed Consent Form for Subjects

Study Title: Assessment of maternal outcomes and foetal outcomes secondary to urinary tract infection in pregnancy.

Study Number: _____

Subject's Initials:_____

Subject's Name: _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____

Signature: Or

Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

_____

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Director, Christian Counseling Centre,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

November 23, 2017

Dr. Anjely Pulparampil Sebastian,
PG Registrar,
Department of Medicine III,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Assessment of maternal outcomes and fetal outcomes secondary to symptomatic urinary tract infection in pregnancy.
Dr. Anjely Pulparampil Sebastian Post Graduate Registrar/ Employment Number: 29556, Department of General Medicine/ General Medicine Unit III Dr Sudha Jasmine Rajan, Employment Number: 28296, Professor, Department of General Medicine Unit III, Dr Sowmya Satyendra, Employment number: 28181 Dr Annie Regi, Employment number: 11190, Department of Obstetrics Unit III, Dr. Rita Vijayaselvi, Employment number: 50600, Department of Obstetrics Unit IV, Dr. Santhosh Benjamin, Employment number: 31318, Department of Obstetrics Unit V, Dr. Rani Diana, Employment number: 30969, Department of Microbiology. Mrs. Vishali, Employment Number: 31093, Department of Biostatistics.

Ref: IRB Min. No. 10627 [OBSERVE] dated 03.04.2017

Dear Dr. Anjely Pulparampil Sebastian,
The Institutional Review Board (**Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Assessment of maternal outcomes and fetal outcomes secondary to symptomatic urinary tract infection in pregnancy" on April 03rd 2017.

The Committee reviewed the following documents:

1. IRB Application format
2. Information Sheets.
3. Cvs of Drs. Sudha Jasmine, Sowmya Sathyendra, Annie Regi, Retta, Santhosh, Rani Diana, Visali and Anjely.
4. Data Entry Form
5. No. of documents 1 – 4..

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on April 03rd 2017 in the CK Job Hall, Christian Medical College, Bagayam, Vellore 632002. 2 of 4

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA (Theology), Dr. Min (Clinical Counselling)	Chairperson, Ethics Committee, IRB, Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. Ratna Prabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Dr. Rekha Pai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist
Dr. Jayaprakash Muliyil	BSC, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist & Epidemiologist
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Sowmya Sathyendra	MBBS, MD (Gen. Medicine)	Professor, Medicine III, CMC, Vellore	Internal, Clinician
Dr. Santhanam Sridhar	MBBS, DCH, DNB	Professor, Neonatology, CMC, Vellore	Internal, Clinician
Dr. Thomas V Paul	MBBS, MD, DNB, PhD	Professor,Endocrinology, CMC, Vellore	Internal, Clinician
Dr Sneha Varkki	MBBS, DCH, DNB	Professor, Paediatrics, CMC, Vellore	Internal, Clinician
Dr. Sathish Kumar	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Hc)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Ajith Sivadasan	MD, DM	Professor, Neurological Sciences, CMC, Vellore	Internal, Clinician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Paitabiraman	BSc. DSSA	Social Worker, Vellore	External, Lay Person
Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC, Vellore	Internal, Clinician
Dr. Shyam Kumar NK	MBBS, DMRD, DNB, FRCR, FRANZCR	Professor, Radiology, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Assessment of maternal outcomes and fetal outcomes secondary to symptomatic urinary tract infection in pregnancy" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of 16,500/- INR (Rupees Sixteen Thousand five hundred only) will be granted for 11 months.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS, MD, DM
SECRETARY (ETHICS COMMITTEE)
INSTITUTIONAL REVIEW BOARD
Christian Medical College, Vellore - 632 002

IRB Min. No. 10627 [OBSERVE] dated 03.04.2017

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

DATA ENTRY SET

SLNO	PROTOCOL	AGE	G	P	L	A	D	SB	ECTOPIC	IUD	PARITY	PREG	FERTILIT
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4	1	30	2	1	1	0	0	0	0	0	2	1	2
5	1	29	3	1	1	1	0	0	0	0	2	1	2
6	1	30	1	0	0	0	0	0	0	0	1	1	2
7	1	25	1	0	0	0	0	0	0	0	1	1	2
8	1	29	2	1	1	0	0	0	0	0	2	1	2
9	1	21	3	0	0	2	0	0	0	0	2	1	2
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15	1	27	1	0	0	0	0	0	0	0	1	1	2
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85	1	23	2	0	0	1	0	0	0	0	2	1	2
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106	1	27	1	0	0	0	0	0	0	0	1	1	2
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144	2	28	3	1	1	1	0	0	0	0	2	1	2
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147	2	19	1	0	0	0	0	0	0	0	1	1	2
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213	2	23	1	0	0	0	0	0	0	0	1	1	2
214	2	28	1	0	0	0	0	0	0	0	1	1	2
215	2	22	3	1	1	1	0	0	0	0	2	1	2
216	2	28	1	0	0	0	0	0	0	0	1	1	2
217	2	24	1	0	0	0	0	0	0	0	1	1	2
218	2	28	1	0	0	0	0	0	0	0	1	1	2

219	2	26	2	1	1	0	0	0	0	0	2	1	2
220	2	20	1	0	0	0	0	0	0	0	1	1	2
221	2	28	2	1	1	0	0	0	0	0	2	1	2
222	2	31	3	2	2	0	0	0	0	0	2	1	2
223	2	28	1	0	0	0	0	0	0	0	1	1	2
224	2	25	1	0	0	0	0	0	0	0	1	1	2
225	2	26	3	2	1	0	0	1	0	0	2	1	2
226	2	28	3	2	2	0	0	0	0	0	2	1	2
227	2	23	2	1	1	0	0	0	0	0	2	1	2
228	2	24	2	1	1	0	0	0	0	0	1	1	2
229	2	20	1	0	0	0	0	0	0	0	1	1	2
230	2	25	3	1	0	1	1	0	0	0	2	1	2
231	2	20	1	0	0	0	0	0	0	0	1	1	2
232	2	24	2	0	0	1	0	0	0	0	2	1	1
233	2	21	1	0	0	0	0	0	0	0	1	1	2
234	2	29	2	1	1	0	0	0	0	0	2	1	2
235	2	27	3	2	1	0	1	0	0	0	2	1	2
236	2	24	3	2	2	0	0	0	0	0	2	1	2
237	2	35	4	3	3	0	0	0	0	0	2	1	2
238	2	29	3	2	1	0	1	0	0	0	2	1	2
239	2	28	1	0	0	0	0	0	0	0	1	1	2
240	2	26	2	1	1	0	0	0	0	0	2	1	2
241	2	26	1	0	0	0	0	0	0	0	1	1	1
242	2	29	1	0	0	0	0	0	0	0	1	1	2
243	2	27	1	0	0	0	0	0	0	0	1	1	2
244	2	22	2	1	1	0	0	0	0	0	2	1	2
245	2	28	2	1	1	0	0	0	0	0	2	1	2
246	2	30	2	1	1	0	0	0	0	0	2	1	2
247	2	24	2	1	1	0	0	0	0	0	2	1	2
248	2	22	1	0	0	0	0	0	0	0	1	1	2
249	2	27	1	0	0	0	0	0	0	0	1	1	2
250	2	24	2	1	1	0	0	0	0	0	2	1	2
251	2	27	2	1	0	0	0	1	0	0	2	1	2
252	2	19	1	0	0	0	0	0	0	0	1	1	2
253	2	29	3	1	1	1	0	0	0	0	2	1	2
254	2	27	1	0	0	0	0	0	0	0	1	1	2
255	2	31	4	1	1	2	0	0	0	0	2	1	2
256	2	30	3	1	1	1	0	0	0	0	2	1	2
257	2	30	3	1	1	1	0	0	0	0	2	1	1
258	2	34	4	3	3	0	0	0	0	0	2	1	2
259	2	31	1	0	0	0	0	0	0	0	1	1	2
260	2	38	1	0	0	0	0	0	0	0	1	1	1
261	2	24	1	0	0	0	0	0	0	0	1	1	2
262	2	21	1	0	0	0	0	0	0	0	1	1	2
263	2	24	1	0	0	0	0	0	0	0	1	1	2
264	2	22	3	1	1	1	0	0	0	0	2	1	2
265	2	32	4	1	1	2	0	0	0	0	2	1	2
266	2	35	3	2	0	0	1	1	0	0	2	1	2
267	2	23	1	0	0	0	0	0	0	0	1	1	2
268	2	26	1	0	0	0	0	0	0	0	1	1	2
269	2	26	1	0	0	0	0	0	0	0	1	1	2
270	2	24	1	0	0	0	0	0	0	0	1	1	2
271	2	18	1	0	0	0	0	0	0	0	1	1	2
272	2	21	3	0	0	2	0	0	0	0	2	1	2
273	2	28	2	1	1	0	0	0	0	0	2	1	2
274	2	26	1	0	0	0	0	0	0	0	1	1	2
275	2	28	1	0	0	0	0	0	0	0	1	1	2
276	2	35	2	1	1	0	0	0	0	0	2	1	2
277	2	36	1	0	0	0	0	0	0	0	1	1	2
278	2	35	1	0	0	0	0	0	0	0	1	1	1
279	2	29	3	1	1	1	0	0	0	0	2	1	2
280	2	23	1	0	0	0	0	0	0	0	1	1	2
281	2	26	1	0	0	0	0	0	0	0	1	1	1
282	2	27	1	0	0	0	0	0	0	0	1	1	2
283	2	28	3	1	1	1	0	0	0	0	2	1	2
284	2	25	3	2	2	0	0	0	0	0	2	1	2
285	2	18	1	0	0	0	0	0	0	0	1	1	2
286	2	26	2	1	1	0	0	0	0	0	2	1	2
287	2	31	1	0	0	0	0	0	0	0	1	1	2
288	2	20	1	0	0	0	0	0	0	0	1	1	2
289	2	35	1	0	0	0	0	0	0	0	1	1	2
290	2	29	2	1	1	0	0	0	0	0	2	1	2
291	1	29	4	1	1	2	0	0	0	0	2	1	2

292	1	31	1	0	0	0	0	0	0	0	1	1	1
293	1	24	1	0	0	0	0	0	0	0	1	1	2
294	1	33	4	2	1	1	1	0	0	0	2	1	2
295	1	22	1	0	0	0	0	0	0	0	1	1	2
296	1	24	1	0	0	0	0	0	0	0	1	1	2
297	1	28	3	1	0	2	0	0	0	0	2	1	2
298	1	33	4	2	2	1	0	0	0	0	2	1	2
299	1	28	2	1	1	0	0	0	0	0	2	1	2
300	1	28	2	1	1	0	0	0	0	0	2	1	2
301	1	29	2	1	1	0	0	0	0	0	2	1	2
302	1	28	1	0	0	0	0	0	0	0	1	1	2
303	1	24	3	2	1	0	0	1	0	0	2	1	2
304	1	27	1	0	0	0	0	0	0	0	1	2	1
305	1	35	1	0	0	0	0	0	0	0	1	2	1
306	1	29	1	0	0	0	0	0	0	0	1	1	2
307	1	33	5	1	1	3	0	0	0	0	3	1	2
308	1	25	1	0	0	0	0	0	0	0	1	1	2
309	1	29	2	1	1	0	0	0	0	0	2	1	2
310	1	31	2	0	0	1	0	0	0	0	2	1	1
311	1	32	1	0	0	0	0	0	0	0	1	1	2
312	1	29	1	0	0	0	0	0	0	0	1	2	1
313	1	25	1	0	0	0	0	0	0	0	1	1	2
314	1	25	3	0	0	2	0	0	0	0	2	1	2
315	1	27	1	0	0	0	0	0	0	0	1	1	2
316	1	31	1	0	0	0	0	0	0	0	1	1	2
317	1	25	1	0	0	0	0	0	0	0	1	1	2
318	1	26	1	0	0	0	0	0	0	0	1	1	2
319	1	21	1	0	0	0	0	0	0	0	1	1	2
320	1	26	3	2	1	0	0	0	0	0	2	1	2
321	1	30	5	3	1	1	2	0	0	0	3	1	2
322	1	23	1	0	0	0	0	0	0	0	1	1	2
323	1	23	2	1	1	0	0	0	0	0	2	1	2
324	1	27	2	0	0	1	0	0	0	0	2	1	2
325	1	26	1	0	0	0	0	0	0	0	1	1	2
326	1	33	3	1	1	1	0	0	0	0	2	1	2
327	1	27	3	2	2	0	0	0	0	0	2	1	2
328	1	24	1	0	0	0	0	0	0	0	1	1	2
329	1	27	4	1	0	2	0	0	0	1	2	1	2
330	1	24	1	0	0	0	0	0	0	0	1	1	2
331	1	26	3	1	1	1	0	0	0	0	2	1	2
332	1	24	1	0	0	0	0	0	0	0	1	1	2
333	1	23	2	1	1	0	0	0	0	0	2	1	2
334	1	32	2	1	1	0	0	0	0	0	2	1	2
335	1	25	1	0	0	0	0	0	0	0	1	1	2
336	1	30	1	0	0	0	0	0	0	0	1	1	2
337	1	28	6	3	1	2	1	0	0	2	3	1	2
338	1	26	1	0	0	0	0	0	0	0	1	1	2
339	1	30	1	0	0	0	0	0	0	0	1	1	2
340	1	22	1	0	0	0	0	0	0	0	1	1	2
341	1	29	4	1	1	2	0	0	0	0	2	1	2
342	1	23	1	0	0	0	0	0	0	0	1	1	1
343	1	32	3	2	1	0	1	0	0	0	2	1	2
344	1	22	2	1	1	0	0	0	0	0	2	1	2
345	1	26	1	0	0	0	0	0	0	0	1	1	2
346	1	26	1	0	0	0	0	0	0	0	1	1	2
347	1	29	1	0	0	0	0	0	0	0	1	1	2
348	1	21	1	0	0	0	0	0	0	0	1	1	2
349	1	29	3	1	1	1	0	0	0	0	2	1	2
350	1	20	3	1	1	1	0	0	0	0	2	1	2
351	1	19	1	0	0	0	0	0	0	0	1	1	2
352	1	29	1	0	0	0	0	0	0	0	1	1	2
353	1	29	1	0	0	0	0	0	0	0	2	1	2
354	1	31	2	1	1	0	0	0	0	0	2	1	2
355	1	30	2	1	1	0	0	0	0	0	2	1	2
356	1	25	1	0	0	0	0	0	0	0	1	1	2
357	1	31	4	2	2	1	0	0	0	0	2	1	2
358	1	32	3	2	2	0	0	0	0	0	2	1	2
359	1	30	1	0	0	0	0	0	0	0	1	1	2
360	2	32	3	1	1	1	0	0	0	0	2	1	2
361	2	30	2	1	1	0	0	0	0	0	2	1	2
362	2	29	3	2	1	0	1	0	0	0	2	1	2
363	2	33	2	1	1	0	0	0	0	0	2	1	2
364	2	26	5	2	2	2	0	0	0	0	3	1	2

365	2	31	3	1	1	1	0	0	0	0	2	1	2
366	2	21	1	0	0	0	0	0	0	0	1	1	2
367	2	25	1	0	0	0	0	0	0	0	1	1	2
368	2	25	1	0	0	0	0	0	0	0	1	1	2
369	2	27	2	1	1	0	0	0	0	0	2	1	2
370	2	26	2	1	1	0	0	0	0	0	2	1	2
371	2	29	1	0	0	0	0	0	0	#NULL!	1	1	2
372	2	24	2	1	1	0	0	0	0	0	2	1	2
373	2	25	1	0	0	0	0	0	0	0	1	1	2
374	2	22	2	1	1	0	0	0	0	0	2	1	2
375	2	22	2	1	1	0	0	0	0	0	2	1	2
376	2	27	2	0	0	1	0	0	0	0	2	1	2
377	2	23	1	0	0	0	0	0	0	0	1	1	2
378	2	23	3	0	0	2	0	0	0	0	2	1	2
379	2	27	2	1	1	0	0	0	0	0	2	1	2
380	2	25	1	0	0	0	0	0	0	0	1	1	2
381	2	24	1	0	0	0	0	0	0	0	1	1	2
382	2	20	1	0	0	0	0	0	0	0	1	1	2
383	1	25	1	0	0	0	0	0	0	0	1	1	2
384	1	26	1	0	0	0	0	0	0	0	1	1	2
385	1	33	5	1	1	3	0	0	0	0	3	1	2
386	1	26	1	0	0	0	0	0	0	0	1	1	1
387	1	30	1	0	0	0	0	0	0	0	1	1	2
388	1	26	1	0	0	0	0	0	0	0	1	1	2
389	1	23	1	0	0	0	0	0	0	0	1	1	2
390	1	24	1	0	0	0	0	0	0	0	1	1	2
391	1	20	2	0	0	1	0	0	0	0	2	2	2
392	1	28	2	0	0	1	0	0	0	0	2	1	1
393	1	27	1	0	0	0	0	0	0	0	1	1	2
394	1	27	1	0	0	0	0	0	0	0	1	1	2
395	1	27	1	0	0	0	0	0	0	0	1	1	2
396	1	32	1	0	0	0	0	0	0	0	1	1	2
397	1	29	1	0	0	0	0	0	0	0	1	1	2
398	1	27	1	0	0	0	0	0	0	0	1	1	1
399	1	27	3	1	0	1	0	1	0	0	2	1	2
400	1	45	3	0	0	2	0	0	0	0	2	1	2
401	1	23	1	0	0	0	0	0	0	0	1	1	2
402	1	30	1	0	0	0	0	0	0	0	1	1	2
403	1	27	1	0	0	0	0	0	0	0	1	1	2
404	1	23	2	0	0	1	0	0	0	0	2	1	2
405	1	22	1	0	0	0	0	0	0	0	1	1	2
406	1	27	1	0	0	0	0	0	0	0	1	1	2
407	1	23	1	0	0	0	0	0	0	0	1	1	2
408	1	32	3	1	1	1	0	0	0	0	2	1	2
409	1	26	1	0	0	0	0	0	0	0	1	1	2
410	1	24	1	0	0	0	0	0	0	0	1	1	2

CONSABOR	EDUCAT	OCCUP	INCOME	SESSCALE	TRIMESTE	SEXCOURS	GENITOUR	PASTCATH	PASTHIST	HB	GESTDM	PREGESTD	HTN
0	4	5	6	3	2	2	2	2	2	10.7	2	2	2
0	6	6	6	4	#NULL!	3	2	2	2	10.7	2	2	2
0	6	10	12	5	2	2	2	2	2	11.1	2	2	2
0	3	4	3	2	2	3	2	1	2	12.3	2	2	2
0	4	5	3	3	3	2	2	1	2	13.2	2	1	1
0	6	10	12	5	3	2	2	2	2	10.0	1	2	2
0	4	5	4	3	2	2	2	2	2	11.5	2	2	2
0	4	5	3	3	3	2	2	2	2	13.0	2	2	2
2	3	4	3	2	3	3	1	2	2	12.4	2	2	2
0	5	6	6	4	1	3	2	2	2	15.1	2	2	2
0	4	5	6	3	3	3	2	2	2	12.5	2	2	2
0	5	6	6	4	3	3	2	2	2	11.9	1	2	2
0	4	5	3	3	3	3	2	2	2	13.3	2	2	2
2	3	5	4	3	3	4	2	2	2	10.4	2	2	2
0	6	10	12	5	2	3	2	2	2	13.1	1	2	2
0	4	5	4	3	3	3	2	2	2	11.8	2	2	2
0	3	2	2	2	3	2	2	2	2	10.0	2	2	2
0	4	5	4	3	3	5	2	2	2	11.3	2	2	2
0	6	6	10	4	3	3	2	2	1	10.2	2	2	2
0	4	5	3	3	3	3	2	1	2	8.9	2	2	2
0	3	2	2	2	3	2	2	2	2	13.8	1	2	2
0	6	10	10	5	2	6	1	2	2	8.7	1	2	2
0	3	5	4	3	3	4	2	1	2	12.8	2	2	2
2	3	5	4	3	1	2	2	2	2	10.1	2	2	2
0	5	6	6	4	3	4	2	2	2	12.4	2	2	2
0	3	5	3	3	2	3	2	2	2	9.8	2	2	2
0	4	5	4	3	3	6	2	2	2	12.8	1	2	2
0	5	5	4	3	3	2	2	2	2	10.4	2	2	2
0	4	5	4	3	2	3	2	2	2	11.0	2	2	2
0	3	5	3	3	3	3	2	2	2	13.2	2	2	2
0	4	5	4	3	2	6	2	2	2	12.0	1	2	2
0	4	5	4	3	1	3	2	2	2	13.3	2	2	2
0	6	10	12	5	1	2	2	2	2	12.5	2	2	2
0	5	6	6	4	3	2	2	2	2	12.9	2	2	2
0	3	5	6	3	2	2	2	2	2	11.3	2	2	2
0	4	5	4	3	3	3	2	2	2	10.5	2	2	2
0	6	10	12	5	1	2	2	2	2	12.6	2	2	2
0	4	5	6	3	3	4	2	2	2	11.2	1	2	2
0	6	10	6	4	3	2	2	1	2	13.5	1	2	2
0	4	1	2	2	3	4	2	1	2	11.6	2	2	2
0	3	4	3	2	2	3	2	2	2	10.2	2	2	1
0	3	5	6	3	3	3	2	2	2	12.6	1	2	2
2	3	5	4	3	3	3	2	1	2	9.0	2	2	2
0	5	6	6	4	3	3	2	2	2	11.0	1	2	2
0	4	1	6	3	3	4	2	2	2	9.8	2	2	2
0	4	4	4	3	2	3	2	2	2	8.6	2	2	2
2	3	5	4	3	3	5	2	2	2	11.8	1	2	2
0	5	5	3	3	2	3	2	2	2	10.2	1	2	2
0	6	6	6	4	3	3	2	2	2	13.0	2	1	2
0	5	5	4	3	1	3	2	1	2	12.6	2	2	2
0	6	10	12	5	3	4	2	2	2	12.4	1	2	2
0	5	6	6	4	3	4	2	2	2	12.4	2	2	2
0	4	5	6	3	3	4	2	2	2	13.2	1	2	2
0	5	5	3	3	3	5	2	2	2	10.9	2	2	2
0	5	6	6	4	3	4	2	2	2	10.9	1	2	2
0	5	6	6	4	3	4	2	2	2	11.3	2	2	2
0	5	6	6	4	3	4	2	2	2	14.9	2	2	2
0	6	10	12	5	3	2	2	2	2	11.8	2	2	2
0	6	10	12	5	1	5	2	2	2	11.4	2	2	2
0	3	5	6	3	3	5	2	2	2	12.4	2	2	2
0	4	5	6	3	3	2	2	2	2	12.0	2	2	2
0	6	6	6	4	3	3	2	1	2	#NULL!	2	2	2
0	4	5	6	3	3	3	2	2	2	11.0	2	2	2
0	4	5	4	3	3	3	2	2	2	12.3	2	2	2
0	6	6	12	4	1	2	2	1	2	12.0	2	2	2
0	5	5	4	3	3	3	2	2	2	9.1	1	2	2
0	5	6	6	4	3	2	2	2	2	11.4	2	2	2
0	4	5	4	3	3	3	2	2	2	13.2	2	2	2
0	4	5	4	3	3	3	2	2	2	10.6	2	2	2
0	6	6	12	4	1	#NULL!	2	2	2	13.0	2	2	2
0	3	4	3	2	1	4	2	2	2	14.6	2	2	2
0	6	10	12	5	1	2	2	2	2	11.8	2	2	2

0	4	5	4	3	2	3	2	2	2	11.4	2	2	2
0	5	6	4	3	3	3	2	2	2	11.6	1	2	2
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IUGR	GESTBRT	MOOBRTH	APGAR1M	APGAR5M	BABYDEAT	BORN	NICU
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2	39.4	2.66	9	10	2	1	2
2	40.6	3.07	9	10	2	1	2
2	37.0	2.96	9	10	2	1	2
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2	39.3	3.11	9	10	2	1	2
1	38.4	2.30	9	10	2	1	2
2	39.1	3.11	9	10	2	1	2
2	37.2	3.13	9	10	2	1	2
2	39.0	2.97	9	10	2	1	2
2	34.0	2.13	9	10	2	1	1
2	40.3	3.01	4	7	2	1	1
2	31.6	1.42	9	10	2	1	1
2	39.4	2.83	9	10	2	1	2
2	40.6	3.03	9	10	2	1	2
2	35.0	2.00	9	10	2	1	2
1	37.4	1.95	9	10	2	1	1
2	36.2	2.32	9	10	2	1	2
2	34.2	2.70	9	9	2	1	1
2	40.0	2.76	9	10	2	1	2
2	38.6	2.92	9	10	2	1	2
2	38.1	3.64	9	10	2	1	1
2	38.3	2.68	9	10	2	1	2
2	36.0	2.84	9	10	2	1	2
2	40.5	3.52	9	10	2	1	2
2	37.2	2.90	9	10	2	1	2
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2	38.6	3.11	9	10	2	1	2
1	40.0	2.52	9	10	2	1	2
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1	37.4	2.33	9	10	2	1	2
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2	40.3	3.99	9	10	2	1	2
2	38.5	3.34	9	10	2	1	2
2	35.4	2.82	9	10	2	1	2
1	36.6	1.74	9	10	2	1	1
#NULL!	22.1	#NULL!	#NULL!	#NULL!	1	2	#NULL!
2	38.2	3.66	9	10	2	1	2
#NULL!	37.0	#NULL!	#NULL!	#NULL!	1	2	#NULL!
2	38.4	3.66	9	10	2	1	2
2	37.0	3.16	9	10	2	1	2
2	40.2	3.29	9	10	2	1	2
2	38.1	3.92	9	10	2	1	2
2	40.2	3.08	9	10	2	1	2
2	37.1	3.20	9	10	2	1	1
2	38.3	2.64	9	10	2	1	2
2	35.3	2.18	9	10	2	1	1
2	37.5	2.67	9	10	2	1	2
2	38.2	3.08	9	10	2	1	2
2	39.1	3.46	9	10	2	1	2
2	38.4	2.94	9	9	2	1	1
1	38.5	2.29	9	10	2	1	2
1	35.2	2.04	8	8	2	1	2
1	37.4	2.09	9	10	2	1	1
2	40.5	3.12	9	10	2	1	2
2	37.3	2.75	9	10	2	1	2
#NULL!	34.2	#NULL!	#NULL!	#NULL!	2	1	#NULL!
2	35.6	2.38	9	10	2	1	1
2	33.0	2.12	9	9	2	1	1
2	40.1	2.90	9	10	2	1	2
2	37.5	2.96	9	10	2	1	2
2	38.6	3.50	9	10	2	1	2
2	39.3	3.84	9	10	2	1	2
2	40.4	3.54	8	9	2	1	1
2	36.6	2.71	9	10	2	1	1
2	38.3	3.27	9	10	2	1	2
2	35.0	2.45	9	10	2	1	2
1	39.1	2.42	9	10	2	1	2

2	40.1	3.16	9	10	2	1	2
2	40.0	2.87	9	10	2	1	2
#NULL!	28.1	#NULL!	#NULL!	#NULL!	1	2	#NULL!
2	38.3	3.02	9	10	2	1	2
1	35.2	1.84	9	10	2	1	1
2	35.6	2.30	9	10	2	1	1
2	35.6	2.14	9	10	2	1	1
2	36.3	2.44	9	10	2	1	2
2	38.1	2.92	9	10	2	1	2
2	39.0	3.01	9	10	2	1	2
2	34.6	2.20	3	8	2	1	1
2	37.0	3.18	9	9	2	1	2
2	40.1	3.40	9	10	2	1	2
2	39.3	2.76	9	10	2	1	2
2	38.2	2.80	9	10	2	1	2
2	32.1	2.24	4	5	2	1	1
1	35.4	1.96	9	10	2	1	1
#NULL!	19.2	#NULL!	#NULL!	#NULL!	1	4	#NULL!
2	39.3	3.16	9	10	2	1	2
1	35.5	2.38	9	10	2	1	2
2	37.3	2.77	9	10	2	1	2
2	37.6	3.25	9	10	2	1	2
1	37.0	2.46	9	10	2	1	2
2	39.3	2.76	9	10	2	1	2
2	36.5	3.17	9	6	2	1	2
2	38.1	3.12	9	10	2	1	2
2	39.1	3.26	9	10	2	1	2
1	32.1	1.62	9	10	2	1	1
2	40.2	2.71	9	10	2	1	2
#NULL!	37.5	#NULL!	#NULL!	#NULL!	2	1	#NULL!
2	38.4	3.10	9	10	2	1	2
2	36.4	3.46	9	10	2	1	2
2	39.1	2.88	6	8	2	1	2
2	38.1	2.94	9	10	2	1	2
2	39.4	2.66	9	10	2	1	2
2	37.0	2.80	9	10	2	1	2
2	38.3	2.62	9	10	2	1	2
2	38.4	2.76	9	10	2	1	2
2	37.4	2.71	9	10	2	1	2
2	37.6	3.41	9	10	2	1	2
2	37.6	2.52	9	10	2	1	2
1	37.6	2.47	9	10	2	1	2
2	40.0	2.98	8	10	2	1	2
2	40.1	3.25	9	10	2	1	2
2	37.6	3.34	9	10	2	1	2
2	38.6	3.61	9	10	2	1	2
2	37.3	2.77	9	10	2	1	2
2	40.4	3.61	9	10	2	1	2
1	35.2	1.87	9	10	2	1	1
2	39.3	3.72	9	10	2	1	2
2	38.0	2.76	9	10	2	1	2
2	38.4	2.91	9	10	2	1	2
2	37.0	2.52	9	10	2	1	2
2	38.6	2.60	9	10	2	1	2
2	39.2	3.09	9	10	2	1	2
2	38.3	2.96	9	10	2	1	2
2	37.1	2.89	9	10	2	1	2
2	38.3	2.86	9	10	2	1	2
2	39.0	2.83	9	10	2	1	2
2	38.4	3.02	9	10	2	1	2
2	39.1	2.80	9	10	2	1	2
2	38.3	3.10	9	10	2	1	2
2	39.2	3.31	9	10	2	1	2
2	38.4	3.45	9	10	2	1	2
2	36.4	2.41	7	8	2	1	1
2	38.3	3.08	9	10	2	1	2
2	37.4	2.76	9	10	2	1	2
2	40.4	3.52	9	10	2	1	2
2	39.5	3.98	9	10	2	1	2
2	36.2	2.63	9	10	2	1	2
2	37.4	2.80	9	10	2	1	2
2	40.0	3.20	8	10	2	1	2
2	38.4	2.93	9	10	2	1	2

2	39.0	3.10	9	10	2	1	2
2	38.2	2.77	9	10	2	1	2
1	38.2	2.46	9	10	2	1	2
1	31.3	2.16	5	9	2	1	1
2	39.5	2.86	9	10	2	1	2
2	40.2	3.45	9	10	2	1	2
2	40.1	3.72	9	10	2	1	2
2	40.1	3.58	9	10	2	1	2
#NULL!	39.4	2.94	#NULL!	#NULL!	2	1	#NULL!
2	39.1	3.04	9	10	2	1	2
2	40.1	2.74	9	10	2	1	2
2	40.0	3.08	9	10	2	1	2
2	38.6	3.30	9	10	2	1	2
2	39.1	3.09	9	10	2	1	2
2	40.0	3.65	9	10	2	1	2
2	39.0	2.55	9	10	2	1	2
2	38.3	2.76	9	10	2	1	2
2	38.3	3.62	9	10	2	1	2
2	38.3	2.99	9	10	2	1	2
2	40.2	3.08	5	8	2	1	2
2	37.4	2.79	9	10	2	1	2
2	38.5	2.74	9	10	2	1	2
2	38.1	3.17	9	10	2	1	2
2	40.1	3.79	9	10	2	1	2
2	39.5	2.91	9	10	2	1	2
2	40.4	3.30	9	10	2	1	2
2	38.0	3.10	9	10	2	1	2
2	39.4	3.64	9	10	2	1	2
2	40.5	3.22	9	10	2	1	2
1	38.1	2.36	6	9	2	1	2
2	39.2	3.24	9	10	2	1	2
2	39.2	3.12	9	10	2	1	2
2	39.6	2.69	9	10	2	1	2
2	37.5	2.76	9	10	2	1	2
1	32.3	2.12	9	10	2	1	1
2	37.0	3.02	9	10	2	1	2
2	40.1	3.22	9	10	2	1	2
1	31.3	1.43	9	10	2	1	1
2	39.6	3.23	9	10	2	1	2
2	38.3	2.98	9	10	2	1	2
2	39.2	3.17	9	10	2	1	2
2	38.1	2.66	9	10	2	1	2
1	38.1	2.43	9	10	2	1	2
2	40.0	2.95	9	10	2	1	2
1	39.1	2.23	9	10	2	1	2
2	38.1	2.75	9	10	2	1	2
1	40.3	2.26	9	10	2	1	2
2	39.1	3.19	9	10	2	1	2
2	39.6	3.02	9	10	2	1	2
2	39.2	2.98	9	10	2	1	2
2	40.0	3.15	9	10	2	1	2
2	39.2	2.89	9	10	2	1	2
2	40.3	2.98	9	10	2	1	2
2	40.3	3.76	9	10	2	1	2
2	38.3	3.13	9	10	2	1	2
2	39.3	3.22	9	10	2	1	2
2	38.6	2.66	9	10	2	1	2
2	37.2	3.18	9	10	2	1	2
#NULL!	25.2	#NULL!	#NULL!	#NULL!	1	2	#NULL!
2	37.5	2.94	9	10	2	1	2
1	36.0	1.98	9	10	2	1	1
2	35.3	2.14	9	10	2	1	2
2	37.2	2.50	9	10	2	1	2
2	39.3	2.80	9	10	2	1	2
2	38.3	3.19	9	10	2	1	2
2	40.2	3.42	9	10	2	1	2
2	37.6	2.82	8	10	2	1	2
2	37.0	2.89	9	10	2	1	2
2	40.0	3.50	9	10	2	1	2
2	40.0	3.64	9	10	2	1	2
2	40.0	2.75	9	10	2	1	2
2	41.0	3.86	9	10	2	1	2
2	37.4	2.92	6	10	2	1	2

2	39.1	2.72	9	10	2	1	2
2	36.1	1.97	9	10	2	1	2
2	38.3	2.79	9	10	2	1	2
2	39.3	2.93	9	10	2	1	2
1	36.6	2.37	9	10	2	1	2
2	38.6	3.20	9	10	2	1	2
2	34.6	2.16	9	10	2	1	1
2	40.4	3.34	9	10	2	1	2
2	40.1	2.64	9	10	2	1	2
2	40.3	3.04	9	10	2	1	2
2	39.0	2.81	9	10	2	1	2
2	39.1	3.06	9	10	2	1	2
2	39.4	2.87	9	10	2	1	2
2	40.0	3.46	9	10	2	1	2
2	38.4	2.55	9	10	2	1	2
2	37.1	2.85	9	10	2	1	2
2	40.2	3.18	9	10	2	1	2
1	38.3	2.47	9	10	2	1	2
2	39.0	3.09	9	10	2	1	2
1	37.4	2.60	9	10	2	1	2
2	40.6	3.34	9	10	2	1	2
2	38.2	3.12	9	10	2	1	2
2	40.1	3.77	8	9	2	1	2
2	37.6	2.70	9	10	2	1	2
2	38.5	2.98	9	10	2	1	2
2	39.2	2.80	9	10	2	1	2
2	40.3	2.98	9	10	2	1	2
2	39.5	2.73	9	10	2	1	2
2	39.5	2.95	9	10	2	1	2
2	39.5	3.36	9	10	2	1	2
2	35.5	2.32	9	10	2	1	2
1	38.1	2.44	9	10	1	3	1
2	33.6	1.54	9	10	2	1	2
2	34.6	2.15	9	10	2	1	1
2	40.4	3.30	9	10	2	1	2
2	38.3	2.63	9	10	2	1	2
2	37.1	3.80	9	10	2	1	2
2	38.3	4.14	9	10	2	1	2
2	38.4	4.14	9	10	2	1	2
2	36.5	2.41	3	4	2	1	1
2	38.1	2.80	9	10	2	1	2
2	34.5	1.94	7	10	2	1	1
#NULL!	30.1	#NULL!	#NULL!	#NULL!	1	2	#NULL!
2	40.4	3.22	9	10	2	1	2
2	39.2	2.80	9	10	2	1	2
1	36.4	2.41	7	8	2	1	2
2	39.1	3.42	6	10	2	1	2
1	32.4	0.97	5	7	2	1	1
1	29.6	1.24	7	8	2	1	1
2	39.4	3.53	9	10	2	1	2
1	35.3	2.12	9	9	2	1	2
2	38.3	2.76	9	10	1	3	2
2	40.3	3.46	9	10	2	1	2
2	38.6	2.59	9	10	2	1	2
2	39.3	3.18	9	10	2	1	2
2	39.5	3.16	9	10	2	1	2
2	38.0	3.15	9	10	2	1	2
2	37.0	3.04	9	10	2	1	2
2	37.5	2.89	9	10	2	1	2
2	39.1	3.16	9	10	2	1	2
2	38.3	2.91	9	10	2	1	2
2	39.3	3.22	9	10	2	1	2
2	39.4	3.10	7	9	2	1	2
1	38.3	2.40	8	10	2	1	2
2	39.4	2.92	9	10	2	1	2
2	37.6	3.26	9	10	2	1	2
2	40.2	2.98	9	10	2	1	2
2	39.4	3.00	9	10	2	1	2
1	37.5	2.40	9	10	2	1	2
1	37.6	2.46	9	10	2	1	2
2	38.2	2.98	9	10	2	1	2
2	36.3	2.82	7	10	2	1	2
2	40.0	3.12	9	10	2	1	2

1	37.0	2.40	9	10	2	1	2
1	35.0	2.08	9	10	2	1	1
2	32.6	1.98	9	10	2	1	1
2	40.5	3.27	9	10	2	1	1
#NULL!	40.0	#NULL!	#NULL!	#NULL!	1	2	#NULL!
1	38.3	2.50	9	10	2	1	2
2	38.3	2.58	9	10	2	1	2
1	39.5	2.48	9	10	2	1	2
2	37.2	2.82	9	10	2	1	1
2	40.1	2.98	9	10	2	1	2
2	36.6	2.44	9	10	2	1	1
2	37.1	3.09	9	10	2	1	2
#NULL!	32.1	#NULL!	#NULL!	#NULL!	2	1	#NULL!
#NULL!	34.6	#NULL!	#NULL!	#NULL!	2	1	#NULL!
2	39.4	3.50	9	10	2	1	2
2	38.3	3.14	9	10	2	1	2
2	39.5	2.66	9	10	2	1	2
2	40.1	2.98	9	10	2	1	2
2	38.5	3.27	9	10	2	1	2
2	38.2	3.00	5	10	2	1	2
#NULL!	36.1	#NULL!	#NULL!	#NULL!	2	1	#NULL!
2	37.5	3.02	9	10	2	1	2
2	37.3	3.05	9	10	2	1	2
2	36.3	2.76	9	10	2	1	1
2	40.3	3.74	9	10	2	1	2
2	39.2	2.86	9	10	2	1	2
2	38.6	2.87	9	10	2	1	2
2	35.4	2.73	9	10	2	1	1
2	38.6	3.04	9	10	2	1	2
2	35.6	3.10	9	10	2	1	2
2	40.3	3.40	9	10	2	1	2
2	38.0	3.45	9	10	2	1	2
2	28.5	0.94	9	10	2	1	1
1	34.6	2.22	9	10	2	1	1
2	38.6	3.40	9	10	2	1	2
2	40.3	3.30	9	10	2	1	2
2	37.3	3.02	8	10	2	1	2
2	31.5	1.42	9	10	2	1	1
1	38.0	2.16	9	10	2	1	2
2	38.4	2.44	9	10	2	1	2
1	37.4	2.64	9	10	2	1	2
2	40.2	3.25	8	9	2	1	2
1	39.6	2.57	9	10	2	1	2
1	40.3	2.48	8	9	2	1	2
2	34.5	1.85	9	10	2	1	1
2	37.1	3.04	9	10	2	1	2
2	36.2	2.66	9	10	2	1	2
2	40.1	3.07	9	10	2	1	2
1	38.2	2.78	9	10	2	1	2
1	40.0	3.12	9	10	2	1	2
2	39.2	3.06	9	10	2	1	2
2	38.3	3.16	9	10	2	1	2
2	39.2	2.83	9	10	2	1	2
2	40.4	3.04	9	10	2	1	2
#NULL!	10.5	#NULL!	#NULL!	#NULL!	1	4	#NULL!
2	32.5	1.60	9	10	2	1	1
2	38.5	2.36	9	10	2	1	2
1	36.2	1.91	9	10	2	1	1
2	38.1	2.69	9	10	2	1	2
2	40.0	2.96	1	6	2	1	1
2	38.2	2.86	9	10	2	1	2
2	32.0	1.70	9	9	2	1	1
2	37.0	3.05	9	10	2	1	2
1	37.4	1.98	9	10	2	1	1
2	39.5	3.30	9	10	2	1	2
2	39.6	3.46	9	10	2	1	2
2	35.5	2.53	9	10	2	1	2
2	36.6	2.44	9	10	2	1	2
1	37.0	2.40	9	10	2	1	2
2	40.3	2.54	9	10	2	1	2
2	38.3	3.22	9	10	2	1	2
2	39.1	2.80	9	10	2	1	2
2	40.2	2.68	9	10	2	1	2

2	38.4	2.97	9	10	2	1	2
2	39.2	3.08	9	10	2	1	2
2	39.2	3.36	9	10	2	1	2
2	39.1	2.54	9	10	2	1	2
2	39.6	3.00	9	10	2	1	1
2	37.3	2.67	9	10	2	1	1
2	37.3	2.76	9	10	2	1	2
2	38.4	2.80	9	10	2	1	2
2	39.3	3.20	9	10	2	1	2
2	38.1	3.50	9	10	2	1	2
2	39.2	2.72	9	10	2	1	2
2	37.5	2.89	9	10	2	1	2
2	35.5	2.25	9	10	2	1	2
2	39.6	3.96	9	10	2	1	2
2	37.5	3.12	8	9	2	1	2
1	38.1	2.25	9	10	2	1	2
2	39.3	3.22	9	10	2	1	2
2	40.3	3.04	9	10	2	1	2
2	38.0	2.63	9	10	2	1	2
2	35.2	2.39	9	10	2	1	1
2	35.4	2.07	9	10	2	1	2
2	39.2	2.80	9	10	2	1	2
2	40.1	3.10	8	8	2	1	1
2	39.1	3.10	9	10	2	1	2
1	38.4	2.85	9	10	2	1	2
2	34.6	2.06	9	10	2	1	1
#NULL!	33.5	#NULL!	#NULL!	#NULL!	2	1	#NULL!
1	36.1	1.74	9	10	2	1	1
1	38.0	1.92	9	7	2	1	1
2	38.4	3.66	9	10	2	1	2
2	40.2	3.52	9	10	2	1	2
#NULL!	22.1	#NULL!	#NULL!	#NULL!	1	2	#NULL!
2	36.5	3.00	9	10	2	1	2
2	39.4	3.61	9	10	2	1	2
1	37.1	2.14	9	10	2	1	2
2	37.2	2.79	9	10	2	1	2
2	39.6	3.50	9	10	2	1	2
2	40.5	3.25	9	10	2	1	2
2	34.2	2.47	9	10	2	1	1
2	34.2	1.91	9	10	2	1	1
2	38.3	3.07	9	10	2	1	2
2	37.6	2.83	9	10	2	1	2
2	39.6	3.15	9	10	2	1	2
2	35.2	2.30	9	10	2	1	1
2	39.4	3.56	7	9	2	1	2
1	35.2	2.21	9	10	2	1	1